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                   now available on STN
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 NEWS 18  Dec 17   Adis Clinical Trials Insight now available on STN
 NEWS 19  Jan 29   Simultaneous left and right truncation added to COMPENDEX,
                   ENERGY, INSPEC
 NEWS 20  Feb 13   CANCERLIT is no longer being updated
 NEWS 21  Feb 24   METADEX enhancements
 NEWS 22  Feb 24   PCTGEN now available on STN
 NEWS 23  Feb 24   TEMA now available on STN
 NEWS 24  Feb 26   NTIS now allows simultaneous left and right truncation
 NEWS 25  Feb 26   PCTFULL now contains images
 NEWS 26  Mar 04   SDI PACKAGE for monthly delivery of multifile SDI results
 NEWS 27  Mar 19   APOLLIT offering free connect time in April 2003
 NEWS 28  Mar 20   EVENTLINE will be removed from STN
 NEWS 29  Mar 24   PATDPAFULL now available on STN
 NEWS 30  Mar 24   Additional information for trade-named substances without
                   structures available in REGISTRY
 NEWS 31  Apr 11   Display formats in DGENE enhanced
 NEWS 32  Apr 14   MEDLINE Reload
 NEWS 33  Apr 17   Polymer searching in REGISTRY enhanced
 NEWS 34  Apr 21   Indexing from 1947 to 1956 being added to records in CA/CAPLUS
 NEWS 35  Apr 21   New current-awareness alert (SDI) frequency in
                   WPIDS/WPINDEX/WPIX

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 13:00:42 ON 23 APR 2003

=> file uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'USPATFULL' ENTERED AT 13:01:03 ON 23 APR 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 22 Apr 2003 (20030422/PD)
FILE LAST UPDATED: 22 Apr 2003 (20030422/ED)
HIGHEST GRANTED PATENT NUMBER: US6553568
HIGHEST APPLICATION PUBLICATION NUMBER: US2003074707
CA INDEXING IS CURRENT THROUGH 22 Apr 2003 (20030422/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 22 Apr 2003 (20030422/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

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>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s palmitate and vitamin A
         16902 PALMITATE
         29053 VITAMIN
       3437310 A
          7731 VITAMIN A
                 (VITAMIN(W)A)
L1        2113 PALMITATE AND VITAMIN A
```

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=> s l1 and vitamin e
         29053 VITAMIN
       2099612 E
          9753 VITAMIN E
                 (VITAMIN(W)E)
L2        1484 L1 AND VITAMIN E

=> s l2 and vitamin c
         29053 VITAMIN
       1896340 C
          6092 VITAMIN C
                 (VITAMIN(W)C)
L3         894 L2 AND VITAMIN C

=> s l3 and vitaminB .sub. 3
             5 VITAMINB
       1347524 SUB
       3416035 3
             0 VITAMINB .SUB. 3
                 (VITAMINB(W)SUB(W)3)
L4           0 L3 AND VITAMINB .SUB. 3

=> s l3 and vitamin B .sub. 3
         29053 VITAMIN
       1737653 B
       1347524 SUB
       3416035 3
           203 VITAMIN B .SUB. 3
                 (VITAMIN(W)B(W)SUB(W)3)
L5          99 L3 AND VITAMIN B .SUB. 3

=> s l5 and pd<2000
       2605423 PD<2000
                 (PD<20000000)
L6          21 L5 AND PD<2000

=> d l6 1-21

L6   ANSWER 1 OF 21  USPATFULL
AN     2000:34224  USPATFULL
TI     Dietary food enhancement agent
IN     Bangs, William E., Philadelphia, PA, United States
       Khoo, Chor San Heng, Mt. Laurel, NJ, United States
       Ko, Sandy, Abington, PA, United States
PA     Campbell Soup Company, Camden, NJ, United States (U.S. corporation)
PI     US 6039978              20000321
       WO 9639053  19961212                                          <--
AI     US 1996-716421          19960920 (8)
       WO 1996-US10225         19960606
                               19960920  PCT 371 date
                               19960920  PCT 102(e) date
RLI    Continuation-in-part of Ser. No. US 1995-471202, filed on 6 Jun 1995,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 3160
INCL   INCLM: 424/489.000
       INCLS: 426/072.000; 426/073.000; 426/074.000; 514/905.000
NCL    NCLM:  424/489.000
       NCLS:  426/072.000; 426/073.000; 426/074.000; 514/905.000
IC     [7]
```

ICM: A61K009-14
ICS: A23L001-303; A23L001-304
EXF 426/72; 426/73; 426/74; 514/904; 514/905; 424/489
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 2 OF 21 USPATFULL
AN 2000:12814 USPATFULL
TI Carotenoid-nicotinamide-zinc compositions and methods of treatment using same
IN Pero, Ronald W., Lund, Sweden
PA OXiGENE, Inc., Boston, MA, United States (U.S. corporation)
PI US 6020351 20000201
WO 9706790 19970227 <--
AI US 1998-11332 19980811 (9)
WO 1996-US12790 19960807
19980811 PCT 371 date
19980811 PCT 102(e) date
PRAI US 1995-2314P 19950814 (60)
DT Utility
FS Granted
LN.CNT 762
INCL INCLM: 514/355.000
INCLS: 514/356.000; 514/419.000; 514/763.000; 514/762.000; 424/641.000; 424/643.000
NCL NCLM: 514/355.000
NCLS: 424/641.000; 424/643.000; 514/356.000; 514/419.000; 514/762.000; 514/763.000
IC [6]
ICM: A61K031-455
EXF 514/763; 514/762; 514/355; 514/356; 514/419; 424/641; 424/643
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 21 USPATFULL
AN 1999:163234 USPATFULL
TI Skin care compositions and method of improving skin appearance
IN SaNogueira, Jr., James Pedrosa, Wyoming, OH, United States
Dawes, Nancy Coultrip, Cincinnati, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 6001377 19991214 <--
AI US 1998-61929 19980417 (9)
RLI Continuation-in-part of Ser. No. US 1997-862739, filed on 23 May 1997
DT Utility
FS Granted
LN.CNT 2322
INCL INCLM: 424/401.000
INCLS: 424/489.000; 514/937.000; 514/938.000
NCL NCLM: 424/401.000
NCLS: 424/489.000; 514/937.000; 514/938.000
IC [6]
ICM: A61K007-00
ICS: A61K031-74
EXF 424/78.03; 424/401; 424/489; 514/937; 514/938; 514/947
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 4 OF 21 USPATFULL
AN 1999:159506 USPATFULL
TI Skin care compositions and method of improving skin appearance
IN Sine, Mark Richard, Morrow, OH, United States
SaNogueira, Jr., James Pedrosa, Wyoming, OH, United States
Dawes, Nancy Coultrip, Cincinnati, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S.

corporation)
PI US 5997890 19991207 <--
AI US 1998-56028 19980406 (9)
RLI Continuation-in-part of Ser. No. US 1997-862776, filed on 23 May 1997
DT Utility
FS Granted
LN.CNT 2360
INCL INCLM: 424/401.000
INCLS: 514/937.000; 514/938.000; 514/947.000
NCL NCLM: 424/401.000
NCLS: 514/937.000; 514/938.000; 514/947.000
IC [6]
ICM: A61K007-00
EXF 424/401; 514/938; 514/937; 514/947
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 5 OF 21 USPATFULL
AN 1999:159503 USPATFULL
TI Skin care compositions and method of improving skin appearance
IN Ha, Robert Bao Kim, Milford, OH, United States
Fowler, Timothy John, Cincinnati, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5997887 19991207 <--
AI US 1997-966840 19971110 (8)
DT Utility
FS Granted
LN.CNT 2677
INCL INCLM: 424/401.000
INCLS: 514/937.000; 514/938.000; 514/944.000; 514/844.000; 514/845.000; 514/846.000; 514/847.000; 424/069.000; 424/070.100
NCL NCLM: 424/401.000
NCLS: 424/069.000; 424/070.100; 514/844.000; 514/845.000; 514/846.000; 514/847.000; 514/937.000; 514/938.000; 514/944.000
IC [6]
ICM: A61K007-48
EXF 424/401; 424/69; 424/70.1; 514/937; 514/938; 514/944; 514/844; 514/845; 514/846; 514/847

L6 ANSWER 6 OF 21 USPATFULL
AN 1999:155678 USPATFULL
TI Therapeutic system for dietary health management
IN Khoo, Chor San Heng, Mt. Laurel, NJ, United States
MacNair, R. David, King of Prussia, PA, United States
PA Campbell Soup Company, Camden, NJ, United States (U.S. corporation)
PI US 5994295 19991130 <--
AI US 1997-927076 19970910 (8)
RLI Continuation of Ser. No. US 1995-466893, filed on 6 Jun 1995, now abandoned
DT Utility
FS Granted
LN.CNT 3239
INCL INCLM: 514/002.000
INCLS: 514/023.000; 514/558.000; 514/560.000; 514/533.000
NCL NCLM: 514/002.000
NCLS: 514/023.000; 514/533.000; 514/558.000; 514/560.000
IC [6]
ICM: A61K038-00
ICS: A61K031-70; A61K031-20; A61K031-235
EXF 514/2; 514/23; 514/558; 514/560; 514/533
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 7 OF 21 USPATFULL
AN 1999:137208 USPATFULL
TI Therapeutic system for dietary health management
IN Khoo, Chor San Heng, Mt. Laurel, NJ, United States
MacNair, R. David C., King of Prussia, PA, United States
PA Campbell Soup Company, Camden, NJ, United States (U.S. corporation)
PI US 5977059 19991102 <--
AI US 1997-926432 19970910 (8)
RLI Division of Ser. No. US 1995-466893, filed on 6 Jun 1995, now abandoned
DT Utility
FS Granted
LN.CNT 3081
INCL INCLM: 514/002.000
INCLS: 514/023.000; 514/558.000; 514/560.000; 514/533.000
NCL NCLM: 514/002.000
NCLS: 514/023.000; 514/533.000; 514/558.000; 514/560.000
IC [6]
ICM: A61K038-00
ICS: A61K031-70; A61K031-20; A61K031-235
EXF 514/2; 514/23; 514/558; 514/560; 514/533
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 8 OF 21 USPATFULL
AN 1999:136663 USPATFULL
TI UV protection compositions
IN Robinson, Larry Richard, Loveland, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5976513 19991102 <--
AI US 1999-264139 19990305 (9)
RLI Continuation-in-part of Ser. No. US 1998-174225, filed on 16 Oct 1998, now abandoned
DT Utility
FS Granted
LN.CNT 906
INCL INCLM: 424/059.000
INCLS: 424/060.000; 424/400.000; 424/401.000
NCL NCLM: 424/059.000
NCLS: 424/060.000; 424/400.000; 424/401.000
IC [6]
ICM: A61K007-42
ICS: A61K007-00
EXF 424/59; 424/60; 424/400; 424/401
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 9 OF 21 USPATFULL
AN 1999:132881 USPATFULL
TI Pharmaceutical compositions and methods for improving wrinkles and other skin conditions
IN Murad, Howard, 4316 Marina City Dr., Marina del Rey, CA, United States 90292
PI US 5972999 19991026 <--
AI US 1998-146554 19980903 (9)
RLI Continuation of Ser. No. US 1997-787358, filed on 22 Jan 1997, now patented, Pat. No. US 5804594
DT Utility
FS Granted
LN.CNT 1077
INCL INCLM: 514/474.000
INCLS: 514/557.000; 514/062.000; 514/054.000; 514/801.000; 424/417.000
NCL NCLM: 514/474.000
NCLS: 424/417.000; 514/054.000; 514/062.000; 514/557.000; 514/801.000

IC [6]
ICM: A61K031-715
ICS: A61K031-34; A61K031-19
EXF 514/474; 514/557; 514/801; 514/62; 514/54; 424/417
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 10 OF 21 USPATFULL
AN 1999:132251 USPATFULL
TI Skin care compositions and method of improving skin appearance
IN Sine, Mark Richard, Cincinnati, OH, United States
SaNogueira, Jr., James Pedrosa, Cincinnati, OH, United States
Dawes, Nancy Coultrip, Cincinnati, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5972359 19991026 <--
AI US 1998-61509 19980417 (9)
RLI Continuation-in-part of Ser. No. US 1997-862775, filed on 23 May 1997, now abandoned
DT Utility
FS Granted
LN.CNT 2450
INCL INCLM: 424/401.000
INCLS: 106/428.000; 106/436.000; 424/059.000; 424/060.000; 424/063.000; 424/400.000; 514/847.000; 514/938.000
NCL NCLM: 424/401.000
NCLS: 106/428.000; 106/436.000; 424/059.000; 424/060.000; 424/063.000; 424/400.000; 514/847.000; 514/938.000
IC [6]
ICM: A61K007-00
ICS: A61K007-42; A61K007-021; C09C001-36
EXF 424/59; 424/60; 424/63; 424/400; 424/401; 514/847; 514/938; 106/428; 106/436
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 11 OF 21 USPATFULL
AN 1999:132208 USPATFULL
TI UV protection compositions
IN Robinson, Larry Richard, Loveland, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5972316 19991026 <--
AI US 1999-263017 19990305 (9)
RLI Continuation-in-part of Ser. No. US 1998-174307, filed on 16 Oct 1998, now abandoned
DT Utility
FS Granted
LN.CNT 893
INCL INCLM: 424/059.000
INCLS: 424/060.000; 424/400.000; 424/401.000
NCL NCLM: 424/059.000
NCLS: 424/060.000; 424/400.000; 424/401.000
IC [6]
ICM: A61K007-42
ICS: A61K007-00
EXF 424/59; 424/60; 424/400; 424/401
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 12 OF 21 USPATFULL
AN 1999:128146 USPATFULL
TI Skin care compositions
IN Deckner, George Endel, Cincinnati, OH, United States
SaNogueira, Jr., James Pedrosa, Wyoming, OH, United States

Zukowski, Joseph Michael, Cincinnati, OH, United States
PA Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5968528 19991019 <--
AI US 1997-862774 19970523 (8)
DT Utility
FS Granted
LN.CNT 2109
INCL INCLM: 424/401.000
INCLS: 424/059.000; 514/557.000; 514/574.000; 514/844.000; 514/847.000; 514/937.000
NCL NCLM: 424/401.000
NCLS: 424/059.000; 514/557.000; 514/574.000; 514/844.000; 514/847.000; 514/937.000
IC [6]
ICM: A61K007-00
EXF 424/59; 424/401; 514/557; 514/574; 514/844; 514/847; 514/937
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 13 OF 21 USPATFULL
AN 1999:128104 USPATFULL
TI UV protection compositions
IN Robinson, Larry Richard, Loveland, OH, United States
PA Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5968485 19991019 <--
AI US 1999-263673 19990305 (9)
RLI Continuation-in-part of Ser. No. US 1998-174274, filed on 16 Oct 1998, now abandoned
DT Utility
FS Granted
LN.CNT 903
INCL INCLM: 424/059.000
INCLS: 424/060.000; 424/400.000; 424/401.000
NCL NCLM: 424/059.000
NCLS: 424/060.000; 424/400.000; 424/401.000
IC [6]
ICM: A61K007-42
ICS: A61K007-00
EXF 424/59; 424/60; 424/400; 424/401
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 14 OF 21 USPATFULL
AN 1999:121419 USPATFULL
TI Pharmaceutical compositions and methods for treating acne
IN Murad, Howard, 4316 Marina City Dr., Marina del Rey, CA, United States 90292
PI US 5962517 19991005 <--
AI US 1998-16800 19980130 (9)
PRAI US 1997-36825P 19970131 (60)
DT Utility
FS Granted
LN.CNT 960
INCL INCLM: 514/474.000
INCLS: 514/557.000; 514/801.000; 514/474.000; 514/062.000; 514/054.000; 514/859.000; 514/188.000; 424/417.000
NCL NCLM: 514/474.000
NCLS: 424/417.000; 514/054.000; 514/062.000; 514/188.000; 514/557.000; 514/801.000; 514/859.000
IC [6]
ICM: A61K031-715
ICS: A61K031-34; A61K031-19

EXF 514/188; 514/859; 514/310; 514/557; 514/801; 514/474; 514/62; 514/54; 424/417
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 15 OF 21 USPATFULL
AN 1999:96033 USPATFULL
TI Methods of regulating skin appearance with **vitamin B .sub.3** compound
IN Oblong, John Erich, Cincinnati, OH, United States
Bissett, Donald Lynn, Hamilton, OH, United States
Biedermann, Kimberly Ann, Cincinnati, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5939082 19990817 <--
AI US 1997-834010 19970411 (8)
RLI Continuation-in-part of Ser. No. US 1995-554067, filed on 6 Nov 1995, now patented, Pat. No. US 5833998
PRAI US 1996-16043P 19960423 (60)
US 1996-25242P 19960916 (60)
US 1996-28902P 19961021 (60)
DT Utility
FS Granted
LN.CNT 2003
INCL INCLM: 424/401.000
INCLS: 514/844.000; 514/845.000; 514/846.000; 514/938.000
NCL NCLM: 424/401.000
NCLS: 514/844.000; 514/845.000; 514/846.000; 514/938.000
IC [6]
ICM: A61K007-48
EXF 424/401; 514/844; 514/845; 514/846; 514/938
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 16 OF 21 USPATFULL
AN 1998:108425 USPATFULL
TI Pharmaceutical compositions and methods for improving wrinkles and other skin conditions
IN Murad, Howard, 4316 Marina City Dr., Marina del Rey, CA, United States 90292
PI US 5804594 19980908 <--
AI US 1997-787358 19970122 (8)
DT Utility
FS Granted
LN.CNT 1066
INCL INCLM: 514/474.000
INCLS: 514/557.000; 514/801.000; 514/474.000; 514/062.000; 514/054.000; 424/417.000
NCL NCLM: 514/474.000
NCLS: 424/417.000; 514/054.000; 514/062.000; 514/557.000; 514/801.000
IC [6]
ICM: A61K031-715
ICS: A61K031-34; A61K031-19
EXF 514/54; 514/62; 514/474; 514/557; 514/801; 424/417
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 17 OF 21 USPATFULL
AN 97:99011 USPATFULL
TI Composition for treating hair and method for using the same
IN Cannell, David, New York, NY, United States
Nguyen, Nghi, Middlesex, NJ, United States
PA Cosmair, Inc., New York, NY, United States (U.S. corporation)
PI US 5681554 19971028 <--
AI US 1995-496138 19950628 (8)

DT Utility
FS Granted
LN.CNT 933
INCL INCLM: 424/070.140
INCLS: 424/070.100; 424/070.900; 514/004.000
NCL NCLM: 424/070.140
NCLS: 424/070.100; 424/070.900; 514/004.000
IC [6]
ICM: A61K007-06
ICS: A61K007-075
EXF 424/70.14; 424/70.11; 424/70.27; 424/70.1; 424/70.9; 514/4
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 18 OF 21 USPATFULL
AN 97:68148 USPATFULL
TI Personal product compositions comprising heteroatom containing alkyl aldonamide compounds
IN Vermeer, Robert, Nutley, NJ, United States
PA Lever Brothers Company, Division of Conopco, Inc., New York, NY, United States (U.S. corporation)
PI US 5653970 19970805 <--
AI US 1994-352008 19941208 (8)
DT Utility
FS Granted
LN.CNT 6060
INCL INCLM: 424/070.240
INCLS: 424/070.100; 514/847.000; 510/126.000; 510/135.000
NCL NCLM: 424/070.240
NCLS: 424/070.100; 510/126.000; 510/135.000; 514/847.000
IC [6]
ICM: A61K007-07
ICS: A61K007-075
EXF 424/401; 424/70.31; 424/70.19; 424/70.24
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 19 OF 21 USPATFULL
AN 97:53932 USPATFULL
TI Hair care compositions comprising heteroatom containing alkyl aldonamide compounds
IN Vermeer, Robert, Nutley, NJ, United States
PA Lever Brothers Company, Division of Conopco, Inc., New York, NY, United States (U.S. corporation)
PI US 5641480 19970624 <--
AI US 1994-352309 19941208 (8)
DT Utility
FS Granted
LN.CNT 5444
INCL INCLM: 424/070.240
INCLS: 424/070.100
NCL NCLM: 424/070.240
NCLS: 424/070.100
IC [6]
ICM: A61K007-07
ICS: A61K007-075
EXF 424/70.1; 424/70.13; 424/70.17; 424/70.24
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 20 OF 21 USPATFULL
AN 97:51727 USPATFULL
TI Method for determining diet program effectiveness
IN Chait, Allen, Seattle, WA, United States
Hatton, Dan, Portland, OR, United States

```
        Haynes, R. Brian, Dundas, Canada
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PI      US 5639471              19970617                                <--
AI      US 1995-469516          19950606 (8)
DT      Utility
FS      Granted
LN.CNT 3163
INCL    INCLM: 424/439.000
        INCLS: 424/400.000
NCL     NCLM:  424/439.000
        NCLS:  424/400.000
IC      [6]
        ICM: A61K047-00
EXF     424/439; 424/400; 424/440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 21 OF 21  USPATFULL
AN      88:9741  USPATFULL
TI      Effervescent vitamin-mineral granule preparation
IN      Ashmead, H. DeWayne, Fruit Heights, UT, United States
        Petersen, Robert V., Salt Lake City, UT, United States
PA      Albion International, Inc., Clearfield, UT, United States (U.S.
        corporation)
PI      US 4725427              19880216                                <--
AI      US 1984-589152          19840313 (6)
DT      Utility
FS      Granted
LN.CNT 662
INCL    INCLM: 424/044.000
        INCLS: 514/023.000; 514/167.000; 514/168.000; 514/249.000; 514/251.000;
               514/276.000; 514/345.000; 514/356.000; 514/387.000; 514/458.000;
               514/474.000; 514/492.000; 514/494.000; 514/500.000; 514/502.000;
               514/905.000
NCL     NCLM:  424/044.000
        NCLS:  426/591.000; 514/023.000; 514/167.000; 514/168.000; 514/249.000;
               514/251.000; 514/276.000; 514/345.000; 514/356.000; 514/387.000;
               514/458.000; 514/474.000; 514/492.000; 514/494.000; 514/500.000;
               514/502.000; 514/905.000
IC      [4]
        ICM: A61L009-04
        ICS: A61K031-59; A61K031-28; A61K031-30
EXF     424/44; 424/280
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> s l6 and skin
        162870 SKIN
L7          18 L6 AND SKIN

=> d l7 1-18 bib, kwic

L7   ANSWER 1 OF 18  USPATFULL
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AN 2000:34224 USPATFULL
TI Dietary food enhancement agent
IN Bangs, William E., Philadelphia, PA, United States
Khoo, Chor San Heng, Mt. Laurel, NJ, United States
Ko, Sandy, Abington, PA, United States
PA Campbell Soup Company, Camden, NJ, United States (U.S. corporation)
PI US 6039978 20000321
WO 9639053 19961212 <--
AI US 1996-716421 19960920 (8)
WO 1996-US10225 19960606
19960920 PCT 371 date
19960920 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1995-471202, filed on 6 Jun 1995, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Mosher, Mary E.
LREP Baker & Botts, L.L.P.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1,3
DRWN 4 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 3160
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6039978 20000321
WO 9639053 19961212 <--
AB The invention is a dietary food enhancement agent for fortifying food products. The agent includes a premixed combination of **Vitamin A**, Vitamin B.sub.1, Vitamin B.sub.2, Vitamin B.sub.6, Vitamin B.sub.12, **Vitamin C**, Vitamin D, **Vitamin E**, Vitamin K, Biotin, Calcium, Copper, Folic Acid, Iodine, Iron, Magnesium, Manganese, Pantothenic Acid, Phosphorus, and Zinc. Further, calcium may be. . .
SUMM The NCI also suggests that diets rich in foods containing **Vitamin C** and **Vitamin A** from fruits and vegetables may also reduce the risk of cancer. Epidemiologic studies have shown that diets high in **Vitamin A** and **Vitamin C** are associated with lower risks of some kinds of cancers. Therefore, the NCI recommends consumption of a variety of fruits and vegetables, including fruit and vegetable juices that are high in **Vitamin A** and **Vitamin C**. Especially beneficial are cruciferous vegetables which are good sources of fiber, as well as vitamins and minerals.
DETD . . . major sources of dietary fat rather than by eliminating whole categories of foods. For example, by substituting fish, poultry without **skin**, lean meats and low- or non-fat dairy products for high-fat foods, a patient may lower total fat and SFA intake. . .
DETD TABLE I

	Daily Desired Level of Fortification		
Nutrient	Breakfast Meal (35%)	Lunch Meal (30%)	Dinner Meal (35%)
VITAMIN A, (IU)	1750	1500	1750
VITAMIN D, (IU)	140	120	140
VITAMIN E, (IU)	10.5	9	10.5
VITAMIN C, (mg)	35	30	35
VITAMIN B.sub.1, (mg)	0.53	0.45	0.53
VITAMIN B.sub.2, (mg)	0.6	0.51	0.6
VITAMIN B.sub.3, (mg)	7	6	7
VITAMIN B.sub.6, (mg)	0.7	0.6	0.7
VITAMIN B.sub.12, (mcg)	2.1	1.8	2.1

BIOTIN, (mcg) 105 90. . .

DETD TABLE III

U.S. Recommended Dietary Allowance (USRDA)

NUTRIENT	USRDA
VITAMIN A	5000 IU
VITAMIN B.sub.1	1.5 mg
VITAMIN B.sub.2	1.7 mg
VITAMIN B.sub.3	20 mg NE.sup.1
VITAMIN B.sub.6	2 mg
VITAMIN B.sub.12	6 mcg
VITAMIN C	60 mg
VITAMIN D	400 IU
VITAMIN E	30 IU
VITAMIN K	80 mcg
BIOTIN	300 mcg
CALCIUM	1000 mg
COPPER	2 mg
FOLIC ACID	400 mcg
IODINE. . .	

DETD TABLE IV

DFEA Compositions

NUTRIENT RANGE	CONCENTRATION
VITAMIN A	1125-9900 IU
VITAMIN B.sub.1	0.41-2.07 mg
VITAMIN B.sub.2	0.23-2.24 mg
VITAMIN B.sub.3	6.3-25.3 mg NE
VITAMIN B.sub.6	0.54-2.75 mg
VITAMIN B.sub.12	1.08-8.58 mcg
VITAMIN C	31.5-330 mg
VITAMIN D	36-682 IU
VITAMIN E	9.45-49.5 IU
VITAMIN K	0-110 mcg
BIOTIN	94.5-412.5 mcg
CALCIUM	108-1333.2 mg
COPPER	0.95-3.63 mg
FOLIC ACID	126-660 mcg
IODINE. . .	

DETD TABLE VIII

Vitamin and Mineral Mixture (Frozen Foods)

NUTRIENT	CONCENTRATION	FORM
VITAMIN A	9000 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	1.88 mg	Thiamine Mononitrate
VITAMIN B.sub.2	2.04 mg	Riboflavin
VITAMIN B.sub.3	23 mg NE	Niacinamide
VITAMIN B.sub.6	2.5 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	7.8 mcg	Vitamin B.sub.12
VITAMIN C	300 mg	Ascorbic Acid
VITAMIN D	620 IU	Vitamm D.sub.3
VITAMIN E	45 IU	**Vitamin E** Acetate
VITAMIN K	100 mcg	Vitamin K.sub.1
BIOTIN	375 mcg	Biotin
CALCIUM	1212 mg	Calcium Citrate/ Dicalcium Phosphate

COPPER 3.3. . .

DETD . . . humidity, e.g. in a range of about 35 to 75% RH, to produce a homogenous vitamin mix: 36 mg of **Vitamin A Palmitate** (250 micron spray dried); 300 mg of Ascorbic Acid; 6.2 mg of Vitamin D.sub.3 -100 S.D.; 90 mg of **Vitamin E** acetate 50% (CWS/F); 10 mg of Vitamin K.sub.1, 1% (spray dried); 1.88 mg of Thiamine Mononitrate; 2.04 mg of Riboflavin;. . .

DETD TABLE IX

Vitamin and Mineral Mixture (Cereals)

NUTRIENT	CONCENTRATION	FORM
VITAMIN A	2500 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	0.59 mg	Thiamine Mononitrate
VITAMIN B.sub.2	0.32 mg	Riboflavin
VITAMIN B.sub.3	7.7 mg NE	Niacinamide
VITAMIN B.sub.6	0.84 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	2.4 mcg	Vitamin B.sub.12
VITAMIN C	140 mg	Ascorbic Acid/Sodium Ascorbate
VITAMIN D	80 IU	Vitamin D.sub.3
VITAMIN E	15.75 IU	**Vitamin E** Acetate
VITAMIN K	35 mcg	Vitamin K.sub.1
BIOTIN	141.75 mcg	Biotin
CALCIUM	123.6 mg	Calcium Carbonate
COPPER	1.16 mg	Copper. . .

DETD . . . humidity, e.g. in a range of about 35 to 75% RH, to produce a homogenous vitamin mix: 10 mg of **Vitamin A Palmitate** (250 micron spray dried); 140 mg of Ascorbic Acid; 0.8 mg of Vitamin D.sub.3 -100 S.D.; 31.5 mg of **Vitamin E** acetate 50% (CWS/F); 3.5 mg of Vitamin K.sub.1, 1% (spray dried); 0.59 mg of Thiamine Mononitrate; 0.32 mg of Riboflavin;. . .

DETD TABLE X

Vitamin and Mineral Mixture (Soups and Other Retorted Meals)

NUTRIENT	CONCENTRATION	FORM
VITAMIN A	9000 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	2.63 mg	Thiamine Mononitrate
VITAMIN B.sub.2	2.04 mg	Riboflavin
VITAMIN B.sub.3	23 mg NE	Niacinamide
VITAMIN B.sub.6	2.5 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	7.8 mcg	Vitamin B.sub.12
VITAMIN C	300 mg	Ascorbic Acid
VITAMIN D	620 IU	Vitamin D.sub.3
VITAMIN E	45 IU	**Vitamin E** Acetate
VITAMIN K	100 mcg	Vitamin K.sub.1
BIOTIN	375 mcg	Biotin
CALCIUM	1212 mg	Calcium Citrate/Dicalcium Phosphate
COPPER	3.3 mg. . .	

DETD TABLE XI

Garlic Roll

Nutrient Level	Fortification
VITAMIN A, (IU)	2250
VITAMIN D, (IU)	155
VITAMIN B, (IU)	11.25
VITAMIN C, (mg)	75
VITAMIN B.sub.1, (mg)	0.47
VITAMIN B.sub.2, (mg)	0.51
VITAMIN B.sub.3, (mg NE)	5.75
VITAMIN B.sub.6, (mg)	0.63
VITAMIN B.sub.12, (mcg)	1.95
BIOTIN, (mcg)	93.75
FOLIC ACID, (mcg)	150
PANTOTHENIC ACID,.	. . .

DETD TABLE XII

Raisin Bran Cereal

Nutrient Level	Fortification
VITAMIN A, (IU)	2500
VITAMIN D, (IU)	80
VITAMIN B, (IU)	15.75
VITAMIN C, (mg)	140
VITAMIN B.sub.1, (mg)	0.59
VITAMIN B.sub.2, (mg)	0.32
VITAMIN B.sub.2, (mg NE)	7.7
VITAMIN B.sub.6, (mg)	0.84
VITAMIN.	. .

DETD TABLE XIII

Apple Crisp

Nutrient Level	Fortification
VITAMIN A, (IU)	1620
VITAMIN D, (IU)	111.6
VITAMIN E, (IU)	8.1
VITAMIN C, (mg)	54
VITAMIN B.sub.1, (mg)	0.34
VITAMIN B.sub.2, (mg)	0.37
VITAMIN B.sub.3, (mg NE)	4.14
VITAMIN B.sub.6, (mg)	0.45
VITAMIN B.sub.12, (mcg)	1.4
BIOTIN, (mcg)	67.5
FOLIC ACID, (mcg)	108
PANTOTHENIC ACID,.	. .

DETD TABLE XIV

Whipped Potatoes

Nutrient Level	Fortification
VITAMIN A, (IU)	1080
VITAMIN D, (IU)	74.4
VITAMIN E, (IU)	5.4
VITAMIN C, (mg)	36
VITAMIN B.sub.1, (mg)	0.23
VITAMIN B.sub.2, (mg)	0.25
VITAMIN B.sub.3, (mg NE)	2.76
VITAMIN B.sub.6, (mg)	0.3

VITAMIN B.sub.12, (mcg) 0.94
BIOTIN, (mcg) 45
FOLIC ACID, (mcg) 72
PANTOTHENIC ACID,. . .
DETD TABLE XV

Orange Juice Drink

Fortification

Nutrient Level

VITAMIN A, (IU) 1800
VITAMIN D, (IU) 124
VITAMIN E, (IU) 9
VITAMIN C, (mg) 60
VITAMIN B.sub.1, (mg) 0.38
VITAMIN B.sub.2, (mg) 0.41
VITAMIN B.sub.3, (mg NE) 4.6
VITAMIN B.sub.6, (mg) 0.5
VITAMIN B.sub.12, (mcg) 1.56
BIOTIN, (mcg) 75
FOLIC ACID, (mcg) 120
PANTOTHENIC ACID,. . .
DETD TABLE XVI

Vegetable Soup

Fortification

Nutrient Level

VITAMIN A, (IU) 2700
VITAMIN D, (IU) 186
VITAMIN E, (IU) 13.5
VITAMIN C, (mg) 90
VITAMIN B.sub.1, (mg) 0.79
VITAMIN B.sub.2, (mg) 0.61
VITAMIN B.sub.3, (mg NE) 6.9
VITAMIN B.sub.6, (mg) 0.75
VITAMIN B.sub.12, (mcg) 2.34
BIOTIN, (mcg) 112.1
FOLIC ACID, (mcg) 180
PANTOTHENIC ACID,. . .
DETD TABLE XVII

Fruit Sauce

Fortification

Nutrient Level

VITAMIN A, (IU) 450
VITAMIN D, (IU) 31
VITAMIN E, (IU) 2.25
VITAMIN C, (mg) 15
VITAMIN B.sub.1, (mg) 0.09
VITAMIN B.sub.2, (mg) 0.1
VITAMIN B.sub.3, (mg NE) 1.15
VITAMIN B.sub.6, (mg) 0.13
VITAMIN B.sub.12, (mcg) 0.39
BIOTIN, (mcg) 18.75
FOLIC ACID, (mcg) 30
PANTOTHENIC ACID,. . .
DETD TABLE XVIII

Bagel

Fortification

Nutrient Level

VITAMIN A, (IU) 450
VITAMIN D, (IU) 31
VITAMIN E, (IU) 2.25
VITAMIN C, (mg) 15
VITAMIN B.sub.1, (mg) 0.09
VITAMIN B.sub.2, (mg) 0.1
VITAMIN B.sub.3, (mg NE) 1.15
VITAMIN B.sub.6, (mg) 0.13
VITAMIN B.sub.12, (mcg) 0.39
BIOTIN, (mcg) 18.75
FOLIC ACID, (mcg) 30
PANTOTHENIC ACID,. . .
DETD TABLE XIX

Salisbury Steak
Fortification
Nutrient Level

VITAMIN A, (IU) 2700
VITAMIN D, (IU) 186
VITAMIN E, (IU) 13.5
VITAMIN C, (mg) 90
VITAMIN B.sub.1, (mg) 0.54
VITAMIN B.sub.2, (mg) 0.61
VITAMIN B.sub.3, (mg NE) 6.9
VITAMIN B.sub.6, (mg) 0.75
VITAMIN B.sub.12, (mcg) 2.34
BIOTIN, (mcg) 112.1
FOLIC ACID, (mcg) 180
PANTOTHEMC ACID,. . .
DETD TABLE XX

Salisbury Steak Gravy
Fortification
Nutrient Level

VITAMIN A, (IU) 450
VITAMIN D, (IU) 31
VITAMIN E, (IU) 2.25
VITAMIN C, (mg) 15
VITAMIN B.sub.1, (mg) 0.09
VITAMIN B.sub.2, (mg) 0.1
VITAMIN B.sub.3, (mg NE) 1.15
VITAMIN B.sub.6, (mg) 0.13
VITAMIN B.sub.12, (mcg) 0.39
BIOTIN, (mcg) 18.75
FOLIC ACID, (mcg) 30
PANTOTHENIC ACID,. . .
DETD . . . 7 7 6
Sugar (g) 18 33 35 23
Protein (g) 21 14 16 13
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES
(USRDA)
Vitamin A 35 35 35 35
Vitamin C 55 55 55 55
Calcium 40 40 40 40
Iron 35 35 35 35
Vitamin D 35 35 35 35
Vitamin E 35 35 35 35
Thiamine 35 35 35 35

Riboflavin 35 35 35 35
Niacin 35 35 35 35
Vitamin. . .
DETD . . . 7 5 7
Sugar (g) 9 11 15 11
Protein (g) 19 26 20 20
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)
Vitamin A 30 30 30 30
Vitamin C 50 50 50 50
Calcium 35 35 35 35
Iron 30 30 30 30
Vitamin D 30 30 30 30
Vitamin E 30 30 30 30
Thiamine 30 30 30 30
Riboflavin 30 30 30 30
Niacin 30 30 30 30
Vitamin. . .
DETD . . . 8
Sugar (g) 7 8 6 13 18
Protein (g) 26 24 31 27 33
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)
Vitamin A 35 35 35 35 35
Vitamin C 55 55 55 55 55
Calcium 40 40 40 40 40
Iron 35 35 35 35 35
Vitamin D 35 35 35 35 35
Vitamin E 35 35 35 35 35
Thiamine 35 35 35 35 35
Riboflavin 35 35 35 35 35
Niacin 35 35. . .
DETD . . . 9
Sugar (g) 12 10 11 19 15
Protein (g) 27 28 32 29 25
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)
Vitamin A 35 35 35 35 35
Vitamin C 55 55 55 55 55
Calcium 40 40 40 40 40
Iron 35 35 35 35 35
Vitamin D 35 35 35 35 35
Vitamin E 35 35 35 35 35
Thiamine 35 35 35 35 35
Riboflavin 35 35 35 35 35
Niacin 35 35. . .
DETD . . . 1 3 2
Sugar (g) 2 1 9 11
Protein (g) 6 5 11 10
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)
Vitamin A 4 4 4 4
Vitamin C 4 4 4 4
Calcium 4 4 4 4
Iron 4 4 4 4
Vitamin D 4 4 4 4
Vitamin E 4 4 4 4
Thiamine 4 4 4 4
Riboflavin 4 4 4 4
Niacin 4 4 4 4
Vitamin. . .
DETD . . . life. The trial was also to monitor the safety of the Prepared

Diet by monitoring nutritional intake in plasma vitamins (**Vitamin A** and Vitamin D) and mineral (iron), and trace minerals levels.

CLM What is claimed is:

2. The agent of claim 1, wherein said premixed combination further comprises **Vitamin A**, Vitamin B.sub.1, Vitamin B.sub.2, **Vitamin B.sub.3**, Vitamin B.sub.6, Vitamin B.sub.12, **Vitamin C**, Vitamin D, **Vitamin E**, Vitamin K, biotin, copper, folic acid, iodine, iron, manganese, pantothenic acid, and zinc.

4. The agent of claim 3, wherein said premixed combination further comprises **Vitamin A**, Vitamin B.sub.1, Vitamin B.sub.2, **Vitamin B.sub.3**, Vitamin B.sub.6, Vitamin B.sub.12, **Vitamin C**, Vitamin D, **Vitamin E**, biotin calcium, copper, folic acid, iodine, iron, manganese, pantothenic acid, and zinc.

. . . and stable dietary food enhancement agent for fortifying frozen or retorted food products comprising a premixed combination of sources of **Vitamin A**, Vitamin B.sub.1, Vitamin B.sub.2, **Vitamin B.sub.3**, Vitamin B.sub.6, Vitamin B.sub.12, **Vitamin C**, Vitamin D, **Vitamin E**, Vitamin K, biotin, calcium, copper, folic acid, iodine, iron, magnesium, manganese, pantothenic acid, phosphorus, and zinc, wherein a daily portion in a range of 7.9 to 10 grams comprises: at least about 9000 IU **Vitamin A**; at least about 1.88 mg Vitamin B.sub.1 ; at least about 2.04 mg Vitamin B.sub.2 ; at least about 23 mg **Vitamin B.sub .3** (Niacinamide); at least about 2.5 mg Vitamin B.sub.6 ; at least about 7.8 mcg Vitamin B.sub.12 ; at least about 375 mcg biotin; at least about 1212 mg calcium; at least about 300 mg **Vitamin C**; at least about 3.3 mg copper; at least about 620 IU Vitamin D; at least about 45 IU **Vitamin E**; at least about 600 mcg folic acid; at least about 172.5 mcg iodine; in a range of 5.67 to 20.79. . .

. . . powdered, freeflowing, and stable dietary food enhancement agent for fortifying cereal food products comprising a premixed combination of sources of **Vitamin A**, Vitamin B.sub.1, Vitamin B.sub.2, **Vitamin B.sub.3**, Vitamin B.sub.6, Vitamin B.sub.12, **Vitamin C**, Vitamin D, **Vitamin E**, Vitamin K, biotin, calcium, copper, folic acid, iodine, iron, magnesium, manganese, pantothenic acid, phosphorus, and zinc, wherein a daily portion in a range of 0.86 to 1.6 grams comprises: about 2500 IU **Vitamin A**; about 0.59 mg Vitamin B.sub.1 ; about 0.32 mg Vitamin B.sub.2 ; about 7.7 mg **Vitamin B.sub.3** (Niacinamide); about 0.84 mg Vitamin B.sub.6 ; about 2.4 mcg Vitamin B.sub.12 ; about 141.75 mcg biotin; about 140 mg **Vitamin C**; about 123.6 mg calcium; about 1.16 mg copper; about 80 IU Vitamin D; about 15.75 IU **Vitamin E**; about 210 mcg folic acid; about 60.38 mcg iodine; about 6.62 mg iron; about 4.5 mg pantothenic acid; about 38.63. . .

L7 ANSWER 2 OF 18 USPATFULL

AN 1999:163234 USPATFULL

TI **Skin** care compositions and method of improving **skin** appearance

IN SaNogueira, Jr., James Pedrosa, Wyoming, OH, United States
Dawes, Nancy Coultrip, Cincinnati, OH, United States

PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)

PI US 6001377 19991214 <--
AI US 1998-61929 19980417 (9)
RLI Continuation-in-part of Ser. No. US 1997-862739, filed on 23 May 1997
DT Utility
FS Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Howard, Sharon
LREP Henderson, Loretta J., Allen, George W., Matthews, Armina E.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2322
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI **Skin** care compositions and method of improving **skin** appearance
PI US 6001377 19991214 <--
AB Disclosed are topical compositions which provide good coverage of **skin** imperfections, e.g., pores and uneven **skin** tone, while retaining a natural **skin** appearance. The compositions contain a particulate material having a refractive index of at least about 2, e.g., TiO.sub.2, and a **skin** conditioning component.
SUMM The present invention relates to the field of topical compositions for improving the appearance or other condition of **skin**. More particularly, the invention relates to topical compositions which provide good coverage of **skin** imperfections, e.g., pores and uneven **skin** tone, while retaining a natural **skin** appearance.
SUMM . . . compounds have been described in the art as being useful for regulating fine lines, wrinkles and other forms of undesirable **skin** surface texture. In addition, **Vitamin B .sub.3** compounds, particularly niacinamide, have recently been found to provide measurable benefits in regulating **skin** condition, including regulating fine lines, wrinkles and other forms of uneven or rough surface texture associated with aged or photodamaged **skin**. However, many materials require multiple applications over an extended period to provide such appearance benefits. It would be advantageous to. . . composition which provides a more immediate improvement in the appearance of fine lines, wrinkles, pores and other forms of undesirable **skin** surface texture.
SUMM Particulate materials, including TiO.sub.2, have been included in **skin** care compositions. For example, emulsions may contain TiO.sub.2 as an opacifying agent to provide a white appearance to the emulsion.. . . compositions may employ such particulates to impart a sunscreening effect. Several publications have also disclosed the use of TiO.sub.2 in **skin** care compositions. See, e.g., U.S. Pat. No. 5,223,559 and patent application Nos. DE 245815, WO 94/09756 and JP 08188723. In. . . the Soft-Focus Effect, Cosmetics & Toiletries, Vol. 111, July 1996, pp. 57-61). Emmert discloses that one can mechanically fill in **skin** lines with a reflective substance such as TiO.sub.2. However, Emmert teaches that such reflective materials result in an undesirable mask-like. . .
SUMM . . . as TiO.sub.2, of which the present inventors are aware, either do not provide coverage sufficient to reduce the appearance of **skin** imperfections, or tend to result in unacceptable **skin** whitening or other unnatural appearance when applied to the **skin**. It has now also been found that materials which primarily diffuse light, rather than reflect light, do not provide good coverage of **skin** imperfections when used in amounts which are esthetically acceptable to consumers. More particularly, when used at relatively high concentrations to provide coverage, these materials suffer from unacceptable **skin** whitening.
SUMM . . . have now found that reflective materials such as TiO.sub.2 can be formulated in topical compositions to provide good coverage of

skin imperfections while retaining a generally natural appearance, e.g., without unacceptable **skin** whitening. The compositions are especially suitable for providing an immediate visual improvement in **skin** appearance. It has also now been found that improvements in **skin** appearance can be enhanced by further including in the composition a **skin** conditioning component.

SUMM . . . is an object of the present invention to provide topical compositions suitable for imparting an essentially immediate visual improvement in **skin** appearance. It is another object of the present invention to provide topical compositions containing a reflective particulate material, e.g., TiO.sub.2, which provide desirable coverage of **skin** imperfections such as pores and uneven **skin** tone, while maintaining a natural **skin** appearance (e.g., without unacceptable **skin** whitening). Another object of the present invention is to provide such topical compositions which are additionally useful for regulating **skin** appearance and/or condition, especially regulating textural or tonal discontinuities in **skin** (e.g., pores, fine lines, wrinkles, uneven **skin** color). It is a particular object of the invention to provide such compositions wherein the composition contains a **skin** conditioning component.

SUMM The present invention also relates to methods of improving **skin** appearance and/or condition by topical application of the subject compositions.

SUMM . . . at least about 2 and a neat primary particle size of from about 100 nm to about 300 nm; a **skin** conditioning component; and a topical carrier.

SUMM . . . 2% of the particulate material. Preferred particulates are selected from TiO.sub.2, ZnO, and ZrO, with TiO.sub.2 being more preferred. The **skin** conditioning component is preferably selected from emollients, humectants and moisturizers.

SUMM The compositions are useful for imparting an essentially immediate visual improvement in **skin** appearance, while maintaining a natural **skin** appearance.

SUMM . . . application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the **skin**.

SUMM . . . as used herein, means that the compositions or components thereof so described are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability, allergic response, and the like.

SUMM . . . herein means an amount of a compound, component, or composition sufficient to significantly induce a positive benefit, preferably a positive **skin** appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to. . .

SUMM . . . compositions of the invention are useful for topical application and for providing an essentially immediate (i.e., acute) visual improvement in **skin** appearance following application of the composition to the **skin**. Without intending to be limited by theory, it is believed that this acute **skin** appearance improvement results at least in part from therapeutic coverage or masking of **skin** imperfections by the particulate material. The compositions provide the visual benefits without imparting an unacceptable **skin** appearance such as **skin** whitening.

SUMM More particularly, the compositions of the present invention are useful for regulating **skin** condition, including regulating visible and/or tactile discontinuities in **skin**, including but not limited to visible and/or tactile discontinuities in **skin** texture and/or color, more especially discontinuities associated with **skin** aging. Such discontinuities may be induced or caused by

internal and/or external factors. Extrinsic factors include ultraviolet radiation (e.g., from. . . low humidity, harsh surfactants, abrasives, and the like. Intrinsic factors include chronological aging and other biochemical changes from within the **skin**.

SUMM Regulating **skin** condition includes prophylactically and/or therapeutically regulating **skin** condition. As used herein, prophylactically regulating **skin** condition includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in **skin**. As used herein, therapeutically regulating **skin** condition includes ameliorating, e.g., diminishing, minimizing and/or effacing, such discontinuities. Regulating **skin** condition involves improving **skin** appearance and/or feel, e.g., providing a smoother, more even appearance and/or feel. As used herein, regulating **skin** condition includes regulating signs of aging. "Regulating signs of **skin** aging" includes prophylactically regulating and/or therapeutically regulating one or more of such signs (similarly, regulating a given sign of **skin** aging, e.g., lines, wrinkles or pores, includes prophylactically regulating and/or therapeutically regulating that sign).

SUMM "Signs of **skin** aging" include, but are not limited to, all outward visibly and tactilely perceptible manifestations as well as any other macro or micro effects due to **skin** aging. Such signs may be induced or caused by intrinsic factors or extrinsic factors, e.g., chronological aging and/or environmental damage.. . . not limited to, the development of textural discontinuities such as wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, **skin** lines, crevices, bumps, large pores (e.g., associated with adnexal structures such as sweat gland ducts, sebaceous glands, or hair follicles), scaliness, flakiness and/or other forms of **skin** unevenness or roughness, loss of **skin** elasticity (loss and/or inactivation of functional **skin** elastin), sagging (including puffiness in the eye area and jowls), loss of **skin** firmness, loss of **skin** tightness, loss of **skin** recoil from deformation, discoloration (including undereye circles), blotching, sallowness, hyperpigmented **skin** regions such as age spots and freckles, keratoses, abnormal differentiation, hyperkeratinization, elastosis, collagen breakdown, and other histological changes in the stratum corneum, dermis, epidermis, the **skin** vascular system (e.g., telangiectasia or spider vessels), and underlying tissues, especially those proximate to the **skin**.

SUMM . . . to be understood that the present invention is not to be limited to regulation of the above mentioned "signs of **skin** aging" which arise due to mechanisms associated with **skin** aging, but is intended to include regulation of said signs irrespective of the mechanism of origin. As used herein, "regulating **skin** condition" is intended to include regulation of such signs irrespective of the mechanism of origin.

SUMM The present invention is especially useful for therapeutically regulating visible and/or tactile discontinuities in mammalian **skin**, including discontinuities in **skin** texture and color. For example, the apparent diameter of pores decreases, the apparent height of tissue immediately proximate to pore openings approaches that of the interadnexal **skin**, the **skin** tone/color becomes more uniform, and/or the length, depth, and/or other dimension of lines and/or wrinkles are decreased.

SUMM . . . in essentially neat, powdered form or predispersed in various types of dispersants, including but not limited to isopropyl isostearate, isopropyl **palmitate**, methyl isostearate, Finsolv TN, cyclomethicone, and cyclomethicone and dimethicone copolyols.

SUMM **Skin** Conditioning Component

SUMM Compositions of the invention comprise a safe and effective amount of a **skin** conditioning component comprising one or more **skin**

conditioning compounds. The **skin** conditioning component is useful for lubricating the **skin**, increasing the smoothness and suppleness of the **skin**, preventing or relieving dryness of the **skin**, hydrating the **skin**, and/or protecting the **skin**. The **skin** conditioning enhances the **skin** appearance benefits provided by the particulate material. The **skin** conditioning component is preferably selected from the group consisting of emollients, humectants, moisturizers and mixtures thereof. The **skin** conditioning component is preferably present at a level of at least about 0.1%, more preferably from about 1% to about. . .

SUMM . . . but are not limited to, methyl, isopropyl, and butyl esters of fatty acids such as hexyl laurate, isohexyl laurate, isohexyl **palmitate**, isopropyl **palmitate**, methyl **palmitate**, decyloleate, isodecyl oleate, hexadecyl stearate decyl stearate, isopropyl isostearate, methyl isostearate, diisopropyl adipate, diisohexyl adipate, dihexyldecyl adipate, diisopropyl sebacate, lauryl. . .

SUMM Without intending to be limited by theory, it is believed that the **skin** conditioning component provides a preferred Hydration Factor to the compositions of the present invention. Compositions of the invention tend to have a Hydration Factor of at least zero as measured by the **Skin** Moisturizer Hydration Test. The **Skin** Moisturizer Hydration Test evaluates and compares the in-vivo, hydration efficacy of topical compositions. The test method utilizes a Courage and Khazaka Corneometer 820 PC to measure the electrical capacitance of the **skin** surface. Without being limited by theory, it is believed that the electrical capacitance is an indirect measurement of water presence and therefore **skin** surface hydration.

SUMM The **Skin** Moisturizer Hydration Test is determined using at least 16 subjects in general good health (free of medical conditions, adverse reactions or sensitivities which might affect the **skin** test results). In general, the products to be tested are applied to the forearms of each subject, in an area. . .

SUMM Test Method: Apply the composition to the subject's **skin** as described above. Spread the composition on the test region by rubbing in a circular motion, using a cotted finger until the product has blended into the **skin** completely. Take electrical capacitance values with the comeometer at baseline (before product application) and then 3 hours, and 6 hours. . .

SUMM A comparatively higher comeometer reading indicates higher **skin** surface capacitance and therefore higher **skin** surface water content or hydration. The difference between the corneometer values of reference composition and the test formulation (which have. . .

SUMM . . . the present invention comprise a safe and effective amount of a dermatologically acceptable carrier within which the essential particulate material, **skin** conditioning component, and optional other materials are incorporated to enable the essential materials and optional components to be delivered to the **skin** at an appropriate concentration. The carrier can thus act as a diluent, dispersant, solvent, or the like for the essential. . .

SUMM . . . Science and Technology, 2nd Edition, Vol. 2, pp. 443-465 (1972), incorporated herein by reference. Aerosols are typically applied to the **skin** as a spray-on product.

SUMM . . . acceptable emollient. Such compositions preferably contain from about 2% to about 50% of the emollient. Emollients tend to lubricate the **skin**, increase the smoothness and suppleness of the **skin** , prevent or relieve dryness of the **skin**, and/or protect the **skin**. Emollients are typically water-immiscible, oily or waxy materials. A wide variety of suitable emollients are known and may be used. . .

SUMM . . . mousses. Toilet bars are most preferred since this is the form

of cleansing agent most commonly used to wash the **skin**.
Preferred rinse-off cleansing compositions, such as shampoos, include a delivery system adequate to deposit sufficient levels of actives on the **skin** and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure of such delivery. . .

SUMM As used herein, the term "foundation" refers to a liquid, semi-liquid, semi-solid, or solid **skin** cosmetic which includes, but is not limited to lotions, creams, gels, pastes, cakes, and the like. Typically the foundation is used over a large area of the **skin**, such as over the face, to provide a particular look. Foundations are typically used to provide an adherent base for color cosmetics such as rouge, blusher, powder and the like, and tend to hide **skin** imperfections and impart a smooth, even appearance to the **skin** . Foundations of the present invention include a dermatologically acceptable carrier for the essential particulate material and may include conventional ingredients. . .

SUMM . . . melting point of about 25.degree. C. or less under about one atmosphere of pressure, and are suitable for conditioning the **skin** or hair.

SUMM . . . acids include straight chain, branched chain and aryl carboxylic acids). Nonlimiting examples include diisopropyl sebacate, diisopropyl adipate, isopropyl myristate, isopropyl **palmitate**, methyl **palmitate**, myristyl propionate, 2-ethylhexyl **palmitate**, isodecyl neopentanoate, di-2-ethylhexyl maleate, cetyl **palmitate**, myristyl myristate, stearyl stearate, isopropyl stearate, methyl stearate, cetyl stearate, behenyl behenrate, dioctyl maleate, dioctyl sebacate, diisopropyl adipate, cetyl octanoate,. . .

SUMM . . . additives, cosmetic biocides, denaturants, cosmetic astringents, drug astringents, external analgesics, film formers, opacifying agents, fragrances, perfumes, pigments, colorings, essential oils, **skin** sensates, **skin** soothing agents, **skin** healing agents, pH adjusters, plasticizers, preservatives, preservative enhancers, propellants, reducing agents, **skin** penetration enhancing agents, solvents, suspending agents, emulsifiers, thickening agents, solubilizing agents, polymers for aiding the film-fomning properties and substantivity of. . . anti-androgens, depilation agents, desquamation agents/exfoliants, organic hydroxy acids, vitamins and derivatives thereof (including water dispersible or soluble vitamins such as **Vitamin C** and ascorbyl phosphates), compounds which stimulate collagen production, and natural extracts. Such other materials are known in the art. Nonexclusive. . .

SUMM In a preferred embodiment, the composition also includes an active useful for chronically regulating **skin** condition. Such materials are those which manifest **skin** appearance benefits following chronic application of the composition containing such materials. Materials having this effect include, but are not limited to, **Vitamin B.sub.3** compounds and retinoids.

SUMM A. **Vitamin B.sub.3** Compounds

SUMM In a preferred embodiment, the compositions of the present invention comprise a safe and effective amount of a **vitamin B.sub.3** compound. The **vitamin B.sub.3** compound enhances the **skin** appearance benefits of the present invention, especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores. The compositions of the present invention preferably comprise from about 0.01% to about. . . and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the **vitamin B.sub.3** compound.

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR3## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B.sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM . . . As used herein, "non-vasodilating" means that the ester does not commonly yield a visible flushing response after application to the **skin** in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds. . .

SUMM Other derivatives of the **vitamin B.sub.3** compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of. . .

SUMM . . . esters of the carboxylic acids salicylic acid, acetic acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of **vitamin B.sub.3** compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methyl-nicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid irnide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid,. . .

SUMM Examples of the above **vitamin B.sub.3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM One or more **vitamin B.sub.3** compounds may be used herein. Preferred **vitamin B.sub.3** compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

SUMM . . . and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating **skin** condition described herein.

SUMM Salts of the **vitamin B.sub.3** compound are also useful herein. Nonlimiting examples of salts of the **vitamin B.sub.3** compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide,. . . e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the **vitamin B.sub.3** compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic. . .

SUMM In a preferred embodiment, the ring nitrogen of the **vitamin B.sub.3** compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the **skin** becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the **vitamin B.sub.3** compound is essentially uncomplexed. Therefore, if the composition contains the **vitamin B.sub.3** compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the **skin**. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility. . .

SUMM More preferably the **vitamin B.sub.3** compound is substantially uncomplexed in the composition prior to delivery to the **skin**. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of

materials which form substantially irreversible or other complexes with the **vitamin B.sub.3** compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the **vitamin B.sub.3** compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill. . .

SUMM Thus, in a preferred embodiment, the **vitamin B.sub.3** compound contains a limited amount of the salt form and is more preferably substantially free of salts of a **vitamin B.sub.3** compound. Preferably the **vitamin B.sub.3** compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The **vitamin B.sub.3** compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about. . .

SUMM The **vitamin B.sub.3** compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The **vitamin B.sub.3** compound is preferably substantially pure, more preferably essentially pure.

SUMM In a preferred embodiment, the compositions of the present invention contain a retinoid. The retinoid enhances the **skin** appearance benefits of the present invention, especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores.

SUMM As used herein, "retinoid" includes all natural and/or synthetic analogs of **Vitamin A** or retinol-like compounds which possess the biological activity of **Vitamin A** in the **skin** as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably retinol, retinol esters (e.g., C.sub.2 -C.sub.22 alkyl esters of retinol, including retinyl **palmitate**, retinyl acetate, retinyl propionate), retinal, and/or retinoic acid (including all-trans retinoic acid and/or 13-cis-retinoic acid), more preferably retinoids other than. . . adapalene {6-[3-(1-adamantyl)-4-metboxyphenyl]-2-naphthoic acid}, and tazarotene (ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)-ethynyl]nicotinate). One or more retinoids may be used herein. Preferred retinoids are retinol, retinyl **palmitate**, retinyl acetate, retinyl proprionate, retinal and combinations thereof. More preferred are retinol and retinyl **palmitate**.

SUMM . . . contain a safe and effective amount of the retinoid, such that the resultant composition is safe and effective for regulating **skin** condition, preferably for regulating visible and/or tactile discontinuities in **skin**, more preferably for regulating signs of **skin** aging, even more preferably for regulating visible and/or tactile discontinuities in **skin** texture associated with **skin** aging. The compositions preferably contain from or about 0.005% to or about 2%, more preferably 0.01% to or about 2%,. . .

SUMM In a preferred embodiment, the composition contains both a retinoid and a **Vitamin B.sub.3** compound. The retinoid is preferably used in the above amounts, and the **vitamin B.sub.3** compound is preferably used in an amount of from or about 0.1% to or about 10%, more preferably from or. . .

SUMM . . . 0.1% to about 10%, more preferably from about 0.5% to about 5%, of the composition. The anti-inflammatory agent enhances the **skin** appearance benefits of the present invention, e.g., such agents contribute to a more uniform and acceptable **skin** tone or color. The exact amount of anti-inflammatory agent to be used in the

compositions will depend on the particular. . .

SUMM An agent may also be added to any of the compositions useful in the subject invention to improve the **skin** substantivity of those compositions, particularly to enhance their resistance to being washed off by water, or rubbed off. A preferred. . .

SUMM . . . which can cause increased scaling or texture changes in the stratum coineum and against other environmental agents which can cause **skin** damage.

SUMM Anti-oxidants/radical scavengers such as ascorbic acid (**vitamin C**) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate), tocopherol (**vitamin E**), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under. . . acid and its salts, lycine pidolate, arginine pilolate, nordihydroguaiaretic acid, bioflavonoids, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape **skin**/seed extracts, melanin, and rosemary extracts may be used. Preferred anti-oxidants/radical scavengers are selected from tocopherol sorbate and other esters of. . .

SUMM . . . of a chelating agent is especially useful for providing protection against UV radiation which can contribute to excessive scaling or **skin** texture changes and against other environmental agents which can cause **skin** damage.

SUMM . . . about 5%, also preferably from about 0.5% to about 2%. Salicylic acid is preferred. The organic hydroxy acids enhance the **skin** appearance benefits of the present invention. For example, the organic hydroxy acids tend to improve the texture of the **skin**.

SUMM . . . about 0.2% to about 5%, also preferably from about 0.5% to about 4% of the composition. Desquamation agents enhance the **skin** appearance benefits of the present invention. For example, the desquamation agents tend to improve the texture of the **skin** (e.g., smoothness). A variety of desquamation agents are known in the art and are suitable for use herein, including but. . .

SUMM I. **Skin** Lightening Agents

SUMM The compositions of the present invention may comprise a **skin** lightening agent. When used, the compositions preferably comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%, of a **skin** lightening agent. Suitable **skin** lightening agents include those known in the art, including kojic acid, arbutin, ascorbic acid and derivatives thereof, e.g., magnesium ascorbyl phosphate. **Skin** lightening agents suitable for use herein also include those described in copending patent application Ser. No. 08/479,935, filed on Jun.. . .

SUMM Methods for Regulating **Skin** Condition

SUMM The compositions of the present invention are useful for regulating mammalian **skin** condition (especially human **skin**, more especially human facial **skin**), including regulating visible and/or tactile discontinuities in **skin**, e.g., visible and/or tactile discontinuities in **skin** texture, more especially discontinuities associated with **skin** aging.

SUMM A wide range of quantities of the compositions of the present invention can be employed to provide a **skin** appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm.sup.2 **skin**, from about 0.1 mg/cm.sup.2 to about 10 mg/cm.sup.2. A particularly useful application amount is about 2 mg/cm.sup.2. Typically applications would. . .

SUMM The compositions of this invention provide a visible improvement in **skin** condition essentially immediately following application of

the composition to the **skin**. Such immediate improvement involves coverage or masking of **skin** imperfections such as textural discontinuities (including those associated with **skin** aging, such as enlarged pores), and/or providing a more even **skin** tone or color.

SUMM In a preferred embodiment, the composition includes an active which chronically regulates **skin** condition and is topically applied chronically. "Chronic topical application" and the like involves continued topical application of the composition over. . . preferably for at least about six months, and more preferably still for at least about one year. Chronic regulation of **skin** condition involves improvement of **skin** condition following multiple topical applications of the composition to the **skin**. While benefits are obtainable after various maximum periods of use (e.g., five, ten or twenty years), it is preferred that. . . however application rates can vary from about once per week up to about three times per day or more. Regulating **skin** condition involves topically applying to the **skin** a safe and effective amount of a composition of the present invention. The amount of the composition which is applied,. . . the active levels of a given composition and the level of regulation desired, e.g., in light of the level of **skin** aging present in the subject and the rate of further **skin** aging.

SUMM Regulating **skin** condition is preferably practiced by applying a composition in the form of a **skin** lotion, cream, cosmetic, or the like which is intended to be left on the **skin** for an extended period, for some esthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition). As used herein, "leave-on" compositions exclude rinse-off **skin** cleansing products. After applying the composition to the **skin**, the leave-on composition is preferably left on the **skin** for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at. . .

DETD Apply the composition to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** to provide an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

DETD . . . 6 6
TiO.sub.2 0.75 0.75
Phase C Glycerin 3 3
Carbopol 954 0.4 0.4
EDTA 0.1 0.1
Phase D Cetyl **Palmitate** 1.5 1.5
Cetyl Alcohol 2.25 2.25
Stearyl Alcohol 1.5 1.5
Stearic Acid 0.31 0.31
PEG-100 Stearate 0.31 0.31
Silicone Wax. . . distilled water 0 5
Phase G Glydant Plus 0.1 0.1
distilled water 1 1
glycerin 1 1
Phase H Isopropyl **Palmitate** 1.25 1.25
Retinol 0 0.04
Tween 80 0 0.04
BHT 0 0.05

DETD Apply the composition to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** to provide an essentially immediate visual improvement in **skin** appearance, e.g., reduced

visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

CLM What is claimed:

. . . 100 nm to about 300 nm; (b) from about 1% to about 99% by weight of the composition of a **skin** conditioning component; (c) a topical carier; wherein the total amount of all particulate material in the composition, by weight of. . .

6. The composition of claim 1 wherein the **skin** conditioning component is selected from the group consisting of emollients, humectants, moisturizers and combinations thereof.

7. The composition of claim 1 wherein the composition comprises from about 1% to about 99% of the **skin** conditioning component.

8. The composition of claim 1 wherein the composition comprises from about 5% to about 25% of the **skin** conditioning component.

. . . 100 nm to about 300 nm; (b) from about 2% to about 30% by weight of the composition of a **skin** conditioning component; and (c) a topical carrier.

18. A method of regulating **skin** condition comprising topically applying the composition of claim 1.

19. The method of claim 8, comprising masking imperfections on the **skin** surface.

L7 ANSWER 3 OF 18 USPATFULL

AN 1999:159506 USPATFULL

TI **Skin** care compositions and method of improving **skin** appearance

IN Sine, Mark Richard, Morrow, OH, United States
SaNogueira, Jr., James Pedrosa, Wyoming, OH, United States
Dawes, Nancy Coultrip, Cincinnati, OH, United States

PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)

PI US 5997890 19991207 <--

AI US 1998-56028 19980406 (9)

RLI Continuation-in-part of Ser. No. US 1997-862776, filed on 23 May 1997

DT Utility

FS Granted

EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Howard, Sharon

LREP Allen, George W., Matthews, Armina E., Henderson, Loretta J.

CLMN Number of Claims: 19

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2360

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Skin** care compositions and method of improving **skin** appearance

PI US 5997890 19991207 <--

AB Disclosed are topical compositions which are useful for providing essentially immediate improvements in **skin** appearance, e.g., good coverage of **skin** imperfections, e.g., pores and uneven **skin** tone, in addition to chronic improvements in **skin** appearance, while retaining a natural **skin** appearance. The compositions contain a particulate material having a refractive index of at least about 2, e.g., TiO.sub.2, and an active for regulating

skin condition following multiple topical applications of the composition. Preferred actives include **Vitamin B**. **sub.3** compounds and retinoids.

SUMM The present invention relates to the field of topical compositions for improving the appearance or other condition of **skin**. More particularly, the invention relates to topical compositions which provide good coverage of **skin** imperfections, e.g., pores and uneven **skin** tone, while retaining a natural **skin** appearance.

SUMM . . . compounds have been described in the art as being useful for regulating fine lines, wrinkles and other forms of undesirable **skin** surface texture. In addition, **Vitamin B** .**sub.3** compounds, particularly niacinamide, have recently been found to provide measurable benefits in regulating **skin** condition, including regulating fine lines, wrinkles and other forms of uneven or rough surface texture associated with aged or photodamaged **skin**. However, many materials require multiple applications over an extended period to provide such appearance benefits. It would be advantageous to. . . composition which provides a more immediate improvement in the appearance of fine lines, wrinkles, pores and other forms of undesirable **skin** surface texture.

SUMM Particulate materials, including TiO.sub.2, have been included in **skin** care compositions. For example, emulsions may contain TiO.sub.2 as an opacifying agent to provide a white appearance to the emulsion.. . . compositions may employ such particulates to impart a sunscreening effect. Several publications have also disclosed the use of TiO.sub.2 in **skin** care compositions. See, e.g., U.S. Pat. No. 5,223,559 and patent application Nos. DE 245815, WO 94/09756 and JP 08188723. In. . . the Soft-Focus Effect, Cosmetics & Toiletries, Vol. 111, July 1996, pp. 57-61). Emmert discloses that one can mechanically fill in **skin** lines with a reflective substance such as TiO.sub.2. However, Emmert teaches that such reflective materials result in an undesirable mask-like. . .

SUMM . . . as TiO.sub.2, of which the present inventors are aware, either do not provide coverage sufficient to reduce the appearance of **skin** imperfections, or tend to result in unacceptable **skin** whitening or other unnatural appearance when applied to the **skin**. It has now been found that materials which primarily diffuse light, rather than reflect light, do not provide good coverage of **skin** imperfections when used in amounts which are esthetically acceptable to consumers. More particularly, when used at relatively high concentrations to provide coverage, these materials suffer from unacceptable **skin** whitening.

SUMM . . . have now found that reflective materials such as TiO.sub.2 can be formulated in topical compositions to provide good coverage of **skin** imperfections while retaining a generally natural appearance, e.g., without unacceptable **skin** whitening. The compositions are especially suitable for providing an immediate visual improvement in **skin** appearance. It has also now been found that improvements in **skin** appearance can be enhanced by further including in the composition an active for chronically regulating **skin** condition, e.g., for regulating fine lines, wrinkles, pores and other forms of undesirable **skin** surface texture.

SUMM . . . is an object of the present invention to provide topical compositions suitable for imparting an essentially immediate visual improvement in **skin** appearance. It is another object of the present invention to provide topical compositions containing a reflective particulate material, e.g., TiO.sub.2, which provide desirable coverage of **skin** imperfections such as pores and uneven **skin** tone, while maintaining a natural **skin** appearance (e.g., without unacceptable **skin** whitening).

Another object of the present invention is to provide such topical compositions which are additionally useful for regulating **skin** appearance and/or condition, especially regulating textural or tonal discontinuities in **skin** (e.g., pores, fine lines, wrinkles, uneven **skin** color). It is a particular object of the invention to provide such compositions wherein the composition contains an active for chronically regulating **skin** condition, in addition to the reflective particulate material.

SUMM The present invention also relates to methods of improving **skin** appearance and/or condition by topical application of the subject compositions.

SUMM . . . and a neat primary particle size of from about 100 nm to about 300 nm; an active for chronically regulating **skin** condition; and a topical carrier.

SUMM . . . material. Preferred particulates are selected from TiO.sub.2, ZnO, and ZrO, with TiO.sub.2 being more preferred. Preferred actives for chronically regulating **skin** condition are selected from **Vitamin B.sub.3** compounds, retinoids, and combinations thereof.

SUMM The compositions are useful for imparting an essentially immediate visual improvement in **skin** appearance, along with additional visual improvements in **skin** appearance following multiple topical application of the compositions, while maintaining a natural **skin** appearance.

SUMM . . . application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the **skin**.

SUMM . . . as used herein, means that the compositions or components thereof so described are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability, allergic response, and the like.

SUMM . . . herein means an amount of a compound, component, or composition sufficient to significantly induce a positive benefit, preferably a positive **skin** appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to. . .

SUMM . . . compositions of the invention are useful for topical application and for providing an essentially immediate (i.e.,.acute) visual improvement in **skin** appearance following application of the composition to the **skin**. Without intending to be limited by theory, it is believed that this acute **skin** appearance improvement results at least in part from therapeutic coverage or masking of **skin** imperfections by the particulate material. The compositions of the invention are also useful for providing visual improvements in **skin** appearance or condition following multiple topical applications of the composition to the **skin**. The compositions provide the visual benefits without imparting an unacceptable **skin** appearance such as **skin** whitening.

SUMM More particularly, the compositions of the present invention are useful for regulating **skin** condition, including regulating visible and/or tactile discontinuities in **skin**, including but not limited to visible and/or tactile discontinuities in **skin** texture and/or color, more especially discontinuities associated with **skin** aging. Such discontinuities may be induced or caused by internal and/or external factors. Extrinsic factors include ultraviolet radiation (e.g., from. . . low humidity, harsh surfactants, abrasives, and the like. Intrinsic factors include chronological aging and other biochemical changes from within the **skin**.

SUMM Regulating **skin** condition includes prophylactically and/or therapeutically regulating **skin** condition. As used herein, prophylactically regulating **skin** condition includes delaying, rinimizing and/or preventing visible and/or tactile discontinuities in

skin. As used herein, therapeutically regulating **skin** condition includes ameliorating, e.g., diminishing, minimizing and/or effacing, such discontinuities. Regulating **skin** condition involves improving **skin** appearance and/or feel, e.g., providing a smoother, more even appearance and/or feel. As used herein, regulating **skin** condition includes regulating signs of aging. "Regulating signs of **skin** aging" includes prophylactically regulating and/or therapeutically regulating one or more of such signs (similarly, regulating a given sign of **skin** aging, e.g., lines, wrinkles or pores, includes prophylactically regulating and/or therapeutically regulating that sign).

SUMM "Signs of **skin** aging" include, but are not limited to, all outward visibly and tactilely perceptible manifestations as well as any other macro or micro effects due to **skin** aging. Such signs may be induced or caused by intrinsic factors or extrinsic factors, e.g., chronological aging and/or environmental damage.. . . not limited to, the development of textural discontinuities such as wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, **skin** lines, crevices, bumps, large pores (e.g., associated with adnexal structures such as sweat gland ducts, sebaceous glands, or hair follicles), scaliness, flakiness and/or other forms of **skin** unevenness or roughness, loss of **skin** elasticity (loss and/or inactivation of functional **skin** elastin), sagging (including puffiness in the eye area and jowls), loss of **skin** firmness, loss of **skin** tightness, loss of **skin** recoil from deformation, discoloration (including undereye circles), blotching, sallowness, hyperpigmented **skin** regions such as age spots and freckles, keratoses, abnormal differentiation, hyperkeratinization, elastosis, collagen breakdown, and other histological changes in the stratum corneum, dermis, epidermis, the **skin** vascular system (e.g., telangiectasia or spider vessels), and underlying tissues, especially those proximate to the **skin**.

SUMM . . . to be understood that the present invention is not to be limited to regulation of the above mentioned "signs of **skin** aging" which arise due to mechanisms associated with **skin** aging, but is intended to include regulation of said signs irrespective of the mechanism of origin. As used herein, "regulating **skin** condition" is intended to include regulation of such signs irrespective of the mechanism of origin.

SUMM The present invention is especially useful for therapeutically regulating visible and/or tactile discontinuities in mammalian **skin**, including discontinuities in **skin** texture and color. For example, the apparent diameter of pores decreases, the apparent height of tissue immediately proximate to pore openings approaches that of the interadnexal **skin**, the **skin** tone/color becomes more uniform, and/or the length, depth, and/or other dimension of lines and/or wrinkles are decreased.

SUMM . . . in essentially neat, powdered form or predispersed in various types of dispersants, including but not limited to isopropyl isostearate, isopropyl **palmitate**, methyl isostearate, Finsolv TN, cylcomethicone, and cyclomethicone and dimethicone copolyols.

SUMM Active for Chronically Regulating **Skin** Condition

SUMM The compositions of the invention comprise a safe and effective amount of an active for chronically regulating **skin** condition. Such materials are those which manifest **skin** appearance benefits following chronic application of the composition containing such materials. Materials providing such benefits include, but are not limited to, **Vitamin B.sub.3** compounds, retinoids, and combinations thereof.

SUMM A. **Vitamin B.sub.3** Compounds

SUMM **Vitamin B.sub.3** compounds enhance the **skin** appearance benefits of the present invention,

especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores. The compositions of the present invention preferably comprise from about 0.01% to about. . . and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the **vitamin B.sub.3** compound .

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR1## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B.sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM . . . As used herein, "non-vasodilating" means that the ester does not commonly yield a visible flushing response after application to the **skin** in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds. . .

SUMM Other derivatives of the **vitamin B.sub.3** compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of. . .

SUMM . . . esters of the carboxylic acids salicylic acid, acetic acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of **vitamin B.sub.3** compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methylnicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid,. . .

SUMM Examples of the above **vitamin B.sub.3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM One or more **vitamin B.sub.3** compounds may be used herein. Preferred **vitamin B.sub.3** compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

SUMM . . . and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating **skin** condition described herein.

SUMM Salts of the **vitamin B.sub.3** compound are also useful herein. Nonlimiting examples of salts of the **vitamin B.sub.3** compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide,. . . e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the **vitamin B.sub.3** compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic. . .

SUMM In a preferred embodiment, the ring nitrogen of the **vitamin B.sub.3** compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the **skin** becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the **vitamin B.sub.3** compound is essentially uncomplexed. Therefore, if the composition contains the **vitamin B.sub.3** compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the **skin**. For

example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility. . .

SUMM More preferably the **vitamin B.sub. 3** compound is substantially uncomplexed in the composition prior to delivery to the **skin**. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the **vitamin B.sub.3** compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the **vitamin B.sub. 3** compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill. . .

SUMM Thus, in a preferred embodiment, the **vitamin B. sub.3** compound contains a limited amount of the salt form and is more preferably substantially free of salts of a **vitamin B.sub.3** compound. Preferably the **vitamin B.sub.3** compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The **vitamin B.sub.3** compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about. . .

SUMM The **vitamin B.sub.3** compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The **vitamin B.sub. 3** compound is preferably substantially pure, more preferably essentially pure.

SUMM Retinoids enhance the **skin** appearance benefits of the present invention, especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores.

SUMM As used herein, "retinoid" includes all natural and/or synthetic analogs of **Vitamin A** or retinol-like compounds which possess the biological activity of **Vitamin A** in the **skin** as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably retinol, retinol esters (e.g., C.sub.2 -C.sub.22 alkyl esters of retinol, including retinyl **palmitate**, retinyl acetate, retinyl propionate), retinal, and/or retinoic acid (including all-trans retinoic acid and/or 13-cis-retinoic acid), more preferably retinoids other than. . . adapalene {6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid}, and tazarotene (ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)-ethynyl]nicotinate). One or more retinoids may be used herein. Preferred retinoids are retinol, retinyl **palmitate**, retinyl acetate, retinyl proprionate, retinal and combinations thereof. More preferred are retinol and retinyl **palmitate**.

SUMM . . . contain a safe and effective amount of the retinoid, such that the resultant composition is safe and effective for regulating **skin** condition, preferably for regulating visible and/or tactile discontinuities in **skin**, more preferably for regulating signs of **skin** aging, even more preferably for regulating visible and/or tactile discontinuities in **skin** texture associated with **skin** aging. The compositions preferably contain from or about 0.005% to or about 2%, more preferably 0.01% to or about 2%,. . .

SUMM In a preferred embodiment, the composition contains both a retinoid and a **Vitamin B.sub.3** compound. The retinoid is preferably used in the above amounts, and the **vitamin B.sub.3** compound is preferably used in an amount of from or about 0.1% to or about 10%, more preferably from or. . .

SUMM . . . materials and optional other materials are incorporated to enable the essential materials and optional components to be delivered to the **skin** at an appropriate concentration. The carrier can thus act as a diluent, dispersant, solvent, or the like for the particulate. . .

SUMM . . . Science and Technology, 2nd Edition, Vol. 2, pp. 443-465 (1972), incorporated herein by reference. Aerosols are typically applied to the **skin** as a spray-on product.

SUMM . . . acceptable emollient. Such compositions preferably contain from about 2% to about 50% of the emollient. Emollients tend to lubricate the **skin**, increase the smoothness and suppleness of the **skin** , prevent or relieve dryness of the **skin**, and/or protect the **skin**. Emollients are typically water-immiscible, oily or waxy materials. A wide variety of suitable emollients are known and may be used. . .

SUMM . . . mousses. Toilet bars are most preferred since this is the form of cleansing agent most commonly used to wash the **skin**. Preferred rinse-off cleansing compositions, such as shampoos, include a delivery system adequate to deposit sufficient levels of actives on the **skin** and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure of such delivery. . .

SUMM As used herein, the term "foundation" refers to a liquid, semi-liquid, semi-solid, or solid **skin** cosmetic which includes, but is not limited to lotions, creams, gels, pastes, cakes, and the like. Typically the foundation is used over a large area of the **skin**, such as over the face, to provide a particular look. Foundations are typically used to provide an adherent base for color cosmetics such as rouge, blusher, powder and the like, and tend to hide **skin** imperfections and impart a smooth, even appearance to the **skin** . Foundations of the present invention include a dermatologically acceptable carrier for the essential particulate material and may include conventional ingredients. . .

SUMM . . . melting point of about 25.degree. C. or less under about one atmosphere of pressure, and are suitable for conditioning the **skin** or hair.

SUMM . . . acids include straight chain, branched chain and aryl carboxylic acids). Nonlimiting examples include diisopropyl sebacate, diisopropyl adipate, isopropyl myristate, isopropyl **palmitate**, methyl **palmitate**, myristyl propionate, 2-ethylhexyl **palmitate**, isodecyl neopentanoate, di-2-ethylhexyl maleate, cetyl **palmitate**, myristyl myristate, stearyl stearate, isopropyl stearate, methyl stearate, cetyl stearate, behenyl behenrate, dioctyl maleate, dioctyl sebacate, diisopropyl adipate, cetyl octanoate,. . .

SUMM . . . cosmetic biocides, denaturants, cosmetic astringents, drug astringents, external analgesics, film formers, humectants, opacifying agents, fragrances, perfumes, pigments, colorings, essential oils, **skin** sensates, emollients, **skin** soothing agents, **skin** healing agents, pH adjusters, plasticizers, preservatives, preservative enhancers, propellants, reducing agents, **skin** -conditioning agents, **skin** penetration enhancing agents, **skin** protectants, solvents, suspending agents, emulsifiers, thickening agents, solubilizing agents, polymers for aiding the film-forming properties and substantivity of the composition. . . anti-androgens, depilation agents, desquamation agents/exfoliants, organic hydroxy acids, vitamins and derivatives thereof (including water dispersible or soluble vitamins such as **Vitamin C** and ascorbyl phosphates), compounds which stimulate collagen production, and natural extracts. Such other materials are known in the art. Nonexclusive. . .

SUMM . . . 0.1% to about 10%, more preferably from about 0.5% to about 5%,

of the composition. The anti-inflammatory agent enhances the **skin** appearance benefits of the present invention, e.g., such agents contribute to a more uniform and acceptable **skin** tone or color. The exact amount of anti-inflammatory agent to be used in the compositions will depend on the particular. . .

SUMM An agent may also be added to any of the compositions useful in the subject invention to improve the **skin** substantivity of those compositions, particularly to enhance their resistance to being washed off by water, or rubbed off. A preferred. . .

SUMM . . . which can cause increased scaling or texture changes in the stratum corneum and against other environmental agents which can cause **skin** damage.

SUMM Anti-oxidants/radical scavengers such as ascorbic acid (**vitamin C**) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate), tocopherol (**vitamin E**), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under. . . acid and its salts, lycine pidolate, arginine pilolate, nordihydroguaiaretic acid, bioflavonoids, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape **skin**/seed extracts, melanin, and rosemary extracts may be used. Preferred anti-oxidants/radical scavengers are selected from tocopherol sorbate and other esters of. . .

SUMM . . . of a chelating agent is especially useful for providing protection against UV radiation which can contribute to excessive scaling or **skin** texture changes and against other environmental agents which can cause **skin** damage.

SUMM . . . about 0.2% to about 5%, also preferably from about 0.5% to about 4% of the composition. Desquamation agents enhance the **skin** appearance benefits of the present invention. For example, the desquamation agents tend to improve the texture of the **skin** (e.g., smoothness). A variety of desquamation agents are known in the art and are suitable for use herein, including but. . .

SUMM F. **Skin** Lightening Agents

SUMM The compositions of the present invention may comprise a **skin** lightening agent. When used, the compositions preferably comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%, of a **skin** lightening agent. Suitable **skin** lightening agents include those known in the art, including kojic acid, arbutin, ascorbic acid and derivatives thereof, e.g., magnesium ascorbyl phosphate. **Skin** lightening agents suitable for use herein also include those described in copending patent application Ser. No. 08/479,935, filed on Jun.. . .

SUMM G. **Skin** Conditioners

SUMM Preferred compositions of the invention comprise an optional **skin** conditioning component comprising one or more **skin** conditioning compounds. The **skin** conditioning component is useful for lubricating the **skin**, increasing the smoothness and suppleness of the **skin**, preventing or relieving dryness of the **skin**, hydrating the **skin**, and/or protecting the **skin**. The **skin** conditioning component enhances the **skin** appearance improvements of the present invention, including but not limited to essentially immediate visual improvements in **skin** appearance. The **skin** conditioning component is preferably selected from the group consisting of emollients, humectants, moisturizers and mixtures thereof. The **skin** conditioning component is preferably present at a level of at least about 0.1%, more preferably from about 1% to about. . .

SUMM . . . but are not limited to, methyl, isopropyl, and butyl esters of fatty acids such as hexyl laurate, isohexyl laurate, isohexyl

palmitate, isopropyl **palmitate**, methyl **palmitate**, decyloleate, isodecyl oleate, hexadecyl stearate decyl stearate, isopropyl isostearate, methyl isostearate, diisopropyl adipate, diisohexyl adipate, dihexyldecyl adipate, diisopropyl sebacate, lauryl. . .

SUMM Compositions containing the **skin** conditioning component tend to have a preferred Hydration Factor. Preferred compositions of the present invention have a Hydration Factor of at least zero as measured by the **Skin** Moisturizer Hydration Test. The **Skin** Moisturizer Hydration Test evaluates and compares the in-vivo, hydration efficacy of topical compositions. The test method utilizes a Courage and Khazaka Corneometer 820 PC to measure the electrical capacitance of the **skin** surface. Without being limited by theory, it is believed that the electrical capacitance is an indirect measurement of water presence and therefore **skin** surface hydration.

SUMM The **Skin** Moisturizer Hydration Test is determined using at least 16 subjects in general good health (free of medical conditions, adverse reactions or sensitivities which might affect the **skin** test results). In general, the products to be tested are applied to the forearms of each subject, in an area. . .

SUMM Apply the composition to the subject's **skin** as described above. Spread the composition on the test region by rubbing in a circular motion, using a cotted finger until the product has blended into the **skin** completely. Take electrical capacitance values with the corneometer at baseline (before product application) and then 3 hours, and 6 hours. . .

SUMM A comparatively higher corneometer reading indicates higher **skin** surface capacitance and therefore higher **skin** surface water content or hydration. The difference between the corneometer values of reference composition and the test formulation (which have. . .

SUMM Methods for Regulating **Skin** Condition

SUMM The compositions of the present invention are useful for regulating mammalian **skin** condition (especially human **skin**, more especially human facial **skin**), including regulating visible and/or tactile discontinuities in **skin**, e.g., visible and/or tactile discontinuities in **skin** texture, more especially discontinuities associated with **skin** aging.

SUMM Regulating **skin** condition involves topically applying to the **skin** a safe and effective amount of a composition of the present invention. The amount of the composition which is applied,. . . the active levels of a given composition and the level of regulation desired, e.g., in light of the level of **skin** aging present in the subject and the rate of further **skin** aging.

SUMM A wide range of quantities of the compositions of the present invention can be employed to provide a **skin** appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm.sup.2 **skin**, from about 0.1 mg/cm.sup.2 to about 10 mg/cm.sup.2. A particularly useful application amount is about 2 mg/cm.sup.2. Typically applications would. . .

SUMM The compositions of this invention provide a visible improvement in **skin** condition essentially immediately following application of the composition to the **skin**. Such immediate improvement involves coverage or masking of **skin** imperfections such as textural discontinuities (including those associated with **skin** aging, such as enlarged pores), and/or providing a more even **skin** tone or color.

SUMM The compositions of the invention also provide visible improvements in **skin** condition following chronic topical application of the composition. "Chronic topical application" and the like involves continued topical application of the. . . preferably for at least about six months, and more preferably still for at least about one year.

Chronic regulation of **skin** condition involves improvement of **skin** condition following multiple topical applications of the composition to the **skin**. While benefits are obtainable after various maximum periods of use (e.g., five, ten or twenty years), it is preferred that. . .

SUMM Regulating **skin** condition is preferably practiced by applying a composition in the form of a **skin** lotion, cream, cosmetic, or the like which is intended to be left on the **skin** for an extended period for some esthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition). As used herein, "leave-on" compositions exclude rinse-off **skin** cleansing products. After applying the composition to the **skin**, the leave-on composition is preferably left on the **skin** for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at. . .

DETD Apply the composition to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** to provide an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

DETD . . . B	Glycerin	6	6
	TiO.sub.2	0.75	0.75
Phase C	Glycerin	3	3
	Carbopol 954	0.4	0.4
	EDTA	0.1	0.1
Phase D	Cetyl **Palmitate**	1.5	1.5
	Cetyl Alcohol	2.25	2.25
	Stearyl Alcohol	1.5	1.5
	Stearic Acid	0.31	0.31
	PEG-100 Stearate	0.31	0.31
	Silicone Wax. . .	0	0.5
	distilled water	0	5
Phase G	Glydant Plus	0.1	0.1
	distilled water	1	1
	glycerin	1	1
Phase H	Isopropyl **Palmitate**	1.25	1.25
	Retinol	0	0.04
	Tween 80	0	0.04
	BHT	0	0.05

DETD Apply the composition to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** to provide an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

CLM What is claimed is:

. . . than 100 nm to about 300 nm; (b) a safe and effective amount of an active effective for chronically regulating **skin** condition selected from the group consisting of Vitamin B3 compounds, retinoids, and mixtures thereof; and (c) a topical carrier.

15. The composition of claim 1 comprising a **skin** conditioning component.

. . . of from about 150 nm to about 300 nm; (b) niacinamide in an amount safe and effective for chronically regulating **skin** condition; and (c) a topical carrier.

18. A method of regulating **skin** condition comprising topically applying the composition of claim 1.

19. The method of claim 18, wherein regulating **skin** condition comprises masking or covering textural discontinuities in **skin** and/or providing a more even **skin** tone or color, without whitening the **skin**.

L7 ANSWER 4 OF 18 USPATFULL
AN 1999:159503 USPATFULL
TI **Skin** care compositions and method of improving **skin** appearance
IN Ha, Robert Bao Kim, Milford, OH, United States
Fowler, Timothy John, Cincinnati, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5997887 19991207 <--
AI US 1997-966840 19971110 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Venkat, Jyothsna
LREP Allen, George W., Matthews, Armina E.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2677
TI **Skin** care compositions and method of improving **skin** appearance
PI US 5997887 19991207 <--
AB Disclosed are topical compositions which provide good coverage of **skin** imperfections, e.g., pores and uneven **skin** tone, while retaining a natural **skin** appearance. The compositions contain a charged particulate material dispersed throughout a thickened, hydrophilic carrier. The charged particulate material allows the. . .
SUMM The present invention relates to the field of topical compositions, e.g., **skin** care compositions, suitable for improving the appearance or other condition of **skin**. More particularly, the invention relates to topical **skin** care compositions which provide good coverage of **skin** imperfections, e.g., pores and uneven **skin** tone, while permitting **skin** to retain a natural appearance.
SUMM Consumers have used cosmetic products to care for their **skin** since the dawn of civilization. These products have ranged from simple, commonly-available materials such as honey and plant extracts to,. . .
SUMM Numerous compounds have been described in the art as being useful for regulating **skin** condition, including regulating fine lines, wrinkles and other forms of uneven or rough surface texture associated with aged or photodamaged **skin**. However, many materials require multiple applications over an extended period to provide such appearance benefits. It would be advantageous to. . . composition which provides a more immediate improvement in the appearance of fine lines, wrinkles, pores and other forms of undesirable **skin** surface texture.
SUMM One approach has been to incorporate particulate materials, such as TiO.sub.2, into **skin** care compositions. For example, emulsions may contain TiO2 as an opacifying agent to provide a white appearance to the emulsion.. . . compositions may employ such particulates to

impart a sunscreening effect. Several publications have also disclosed the use of TiO.sub.2 in **skin** care compositions. See, e.g., U.S. Pat. No. 5,223,559 and patent application Nos. DE 245815, WO 94/09756 and JP 08188723. In. . . the Soft-Focus Effect, Cosmetics & Toiletries, Vol. III, July 1996, pp. 57-61). Emmert discloses that one can mechanically fill in **skin** lines with a reflective substance such as TiO.sub.2. However, Emmert teaches that such reflective materials result in an undesirable mask-like. . .

SUMM . . . topical compositions containing reflective materials such as TiO.sub.2, generally either do not provide coverage sufficient to reduce the appearance of **skin** imperfections, or tend to result in unacceptable **skin** whitening or other unnatural appearance when applied to the **skin**. It has also now been found that materials which primarily diffuse light, rather than reflect light, do not provide good coverage of **skin** imperfections when used in amounts which are aesthetically acceptable to consumers. More particularly, when used at relatively high concentrations to provide coverage, these materials suffer from unacceptable **skin** whitening.

SUMM . . . TiO.sub.2, tend to feel dry and add to the negative perception that the composition is not being absorbed into the **skin** and/or that the composition is not providing a **skin** conditioning benefit. As a result, relatively high concentrations contribute to amplify these negative qualities. It has also been found that. . . sufficient coverage, which also adds to the negative perceptions. Thus, it would be desirable to realize aesthetically acceptable degrees of **skin** coverage even though relatively low concentrations of TiO.sub.2 are used.

SUMM In addition, it is desirable for cosmetic compositions to have good aesthetics during application onto the **skin** and while on the **skin**. Good aesthetics means that the composition (i) is light and nongreasy, (ii) has a smooth, silky feel upon the **skin**, (iii) spreads easily, and (iv) absorbs quickly. These desirable aesthetics are often achieved by incorporating thickening agents into a composition.. . . particulate materials, such as metal oxides, are often not compatible with many thickening agents, such as carboxylic acid polymers, and **skin** care actives.

SUMM The present invention overcomes the problems discussed hereinbefore (e.g., unacceptable **skin** whitening, aesthetics, and formulation compatibility issues) by employing charged, surface-treated, reflective particulate materials which are dispersed in a thickened hydrophilic. . . treated reflective particulates (i) are compatible with polymeric thickeners, such as carboxylic acid polymers, (ii) can provide acceptable degrees of **skin** coverage at relatively low concentrations, and (iii) can be formulated into compositions having excellent aesthetics. Such compositions are especially suitable for providing an immediate visual improvement in **skin** appearance when topically applied.

SUMM . . . it is an object of the present invention to provide topical compositions suitable for imparting an immediate visual improvement in **skin** appearance.

SUMM . . . of the present invention to provide topical compositions containing a reflective particulate material, e.g., TiO.sub.2, which provides desirable coverage of **skin** imperfections such as pores and uneven **skin** tone, while maintaining a natural **skin** appearance (e.g., without unacceptable **skin** whitening).

SUMM It is another object of the present invention to provide topical compositions which provide especially effective **skin** coverage while using relatively small amounts of reflective particulate material.

SUMM . . . is yet another object of the present invention is to provide such topical compositions which are additionally useful for regulating **skin** appearance and/or condition, especially regulating textural

or tonal discontinuities in **skin** (e.g., pores and uneven **skin** color).

SUMM It is yet another object of the present invention to provide methods of improving **skin** appearance and/or condition by topical application of the **skin** care compositions described herein.

SUMM The present invention relates to **skin** care compositions which upon topical application to the **skin** provide immediate visual improvement of **skin** appearance. Such compositions comprise: (A) from about 1% to about 99.98%, by weight of the composition, of a hydrophilic liquid. . .

SUMM . . . invention relates to compositions which contain one or more compounds selected from the group consisting of emulsifiers, surfactants, structuring agents, **skin** care actives and combinations thereof.

SUMM The present invention also relates to methods of regulating **skin** condition with the compositions described herein.

SUMM . . . application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the **skin**.

SUMM . . . as used herein, means that the compositions or components thereof so described are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability, allergic response, and the like.

SUMM . . . herein means an amount of a compound, component, or composition sufficient to significantly induce a positive benefit, preferably a positive **skin** appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to. . .

SUMM . . . compositions of the invention are useful for topical application and for providing an essentially immediate (i.e., acute) visual improvement in **skin** appearance following application of the composition to the **skin**. Without intending to be limited by theory, it is believed that this acute **skin** appearance improvement results at least in part from therapeutic coverage or masking of **skin** imperfections by the charged particulate material. The compositions provide the visual benefits without imparting an unacceptable **skin** appearance such as **skin** whitening.

SUMM More particularly, the compositions of the present invention are useful for regulating **skin** condition, including regulating visible and/or tactile discontinuities in **skin**, including but not limited to visible and/or tactile discontinuities in **skin** texture and/or color, more especially discontinuities associated with **skin** aging. Such discontinuities may be induced or caused by internal and/or external factors. Extrinsic factors include ultraviolet radiation (e.g., from. . . low humidity, harsh surfactants, abrasives, and the like. Intrinsic factors include chronological aging and other biochemical changes from within the **skin**.

SUMM Regulating **skin** condition includes prophylactically and/or therapeutically regulating **skin** condition. As used herein, prophylactically regulating **skin** condition includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in **skin**. As used herein, therapeutically regulating **skin** condition includes ameliorating, e.g., diminishing, minimizing and/or effacing, such discontinuities. Regulating **skin** condition involves improving **skin** appearance and/or feel, e.g., providing a smoother, more even appearance and/or feel. As used herein, regulating **skin** condition includes regulating signs of aging. "Regulating signs of **skin** aging" includes prophylactically regulating and/or therapeutically regulating one or more of such signs (similarly, regulating a given sign of **skin** aging, e.g., lines, wrinkles or pores, includes prophylactically regulating and/or

therapeutically regulating that sign).

SUMM "Signs of **skin** aging" include, but are not limited to, all outward visibly and tactilely perceptible manifestations as well as any other macro or micro effects due to **skin** aging. Such signs may be induced or caused by intrinsic factors or extrinsic factors, e.g., chronological aging and/or environmental damage.. . . not limited to, the development of textural discontinuities such as wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, **skin** lines, crevices, bumps, large pores (e.g., associated with adnexal structures such as sweat gland ducts, sebaceous glands, or hair follicles), scaliness, flakiness and/or other forms of **skin** unevenness or roughness, loss of **skin** elasticity (loss and/or inactivation of functional **skin** elastin), sagging (including puffiness in the eye area and jowls), loss of **skin** firmness, loss of **skin** tightness, loss of **skin** recoil from deformation, discoloration (including undereye circles), blotching, sallowness, hyperpigmented **skin** regions such as age spots and freckles, keratoses, abnormal differentiation, hyperkeratinization, elastosis, collagen breakdown, and other histological changes in the stratum corneum, dermis, epidermis, the **skin** vascular system (e.g., telangiectasia or spider vessels), and underlying tissues, especially those proximate to the **skin**.

SUMM . . . to be understood that the present invention is not to be limited to regulation of the above mentioned "signs of **skin** aging" which arise due to mechanisms associated with **skin** aging, but is intended to include regulation of such signs irrespective of the mechanism of origin.

SUMM The present invention is especially useful for therapeutically regulating visible and/or tactile discontinuities in mammalian **skin**, including discontinuities in **skin** texture and color. For example, the apparent diameter of pores decreases, the apparent height of tissue immediately proximate to pore openings approaches that of the interadnexal **skin**, the **skin** tone/color becomes more uniform, and/or the length, depth, and/or other dimension of lines and/or wrinkles are decreased.

SUMM . . . and optional other materials can be incorporated to enable the particulate material and optional components to be delivered to the **skin** at an appropriate concentration. The hydrophilic liquid carrier, thus, ensures that the particulate material is applied to and distributed evenly. . .

SUMM . . . liquid carrier may contain a wide variety of water-soluble or water miscible optional ingredients which can perform one or more **skin** conditioning or **skin** treating functions. Compositions containing a hydrophilic liquid carrier component, which is thickened and which contains the dispersed charged reflective particulate. . .

SUMM . . . phase. As a result, (i) lower concentrations of the reflective particulate material can be used to obtain acceptable degrees of **skin** coverage, (ii) the composition aesthetics are increased, and (iii) formulation instabilities are decreased. Thus, the use of charged particulates provide. . .

SUMM . . . hyaluronate, ammonium hyaluronate, sodium algenate, ammonium algenate, ammonium laurate, sodium laurate, potassium laurate, ammonium myristate, sodium myristate, potassium myristate, ammonium **palmitate**, sodium **palmitate**, potassium **palmitate**, ammonium stearate, sodium stearate, potassium stearate, ammonium oleate, sodium oleate, potassium oleate, and mixtures thereof. More preferred are anionic coating. . .

SUMM The **skin** care compositions of the present invention essentially contain only the thickened, particulate-containing hydrophilic liquid carrier. Preferably, however, the compositions herein,. . .

SUMM . . . acids include straight chain, branched chain and aryl carboxylic acids). Nonlimiting examples include diisopropyl sebacate, diisopropyl adipate, isopropyl myristate, isopropyl **palmitate**, methyl **palmitate**, myristyl propionate, 2-ethylhexyl **palmitate**, isodecyl neopentanoate, di-2-ethylhexyl maleate, cetyl **palmitate**, myristyl myristate, stearyl stearate, isopropyl stearate, methyl stearate, cetyl stearate, behenyl behenate, dioctyl maleate, dioctyl sebacate, diisopropyl adipate, cetyl octanoate,. . .

SUMM . . . Science and Technology, 1st Ed. Knowlton & Pearce (Elsevier 1993). Such ingredients include, but are not limited to, transparent particulates; **skin** conditioning agents such as emollients, humectants, and moisturizers; **skin** cleansers; **skin** care actives such as vitamin B3 compounds, retinoids, anti-oxidants/radical scavengers, and organic hydroxy acids; structuring agents; and other actives including anti-inflammatory agents, sunscreens/sunblocks, chelators, desquamation agents/exfoliants, and **skin** lightening agents. Each of these functional optional ingredients is described in detail as follows:

SUMM 2. **Skin** Care Active: In a preferred embodiment, the composition also includes an active useful for chronically regulating **skin** condition. Such materials are those which manifest **skin** appearance benefits following chronic application of the composition containing such materials. Materials having this effect include, but are not limited to, **Vitamin B**. **sub.3** compounds and retinoids. Other types of **skin** care actives include anti-oxidants/radical scavengers and organic hydroxy acids.

SUMM Specific examples of **skin** care actives include the following.

SUMM (i) **Vitamin B.sub.3** Compounds: In a preferred embodiment, the compositions of the present invention comprise a safe and effective amount of a **vitamin B**. **sub.3** compound. The **vitamin B**. **sub.3** compound enhances the **skin** appearance benefits of the present invention, especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores. The compositions of the present invention preferably comprise from about 0.01% to about. . .

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR3## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B**. **sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM . . . As used herein, "non-vasodilating" means that the ester does not commonly yield a visible flushing response after application to the **skin** in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds. . .

SUMM Other derivatives of the **vitamin B.sub**. **3** compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of. . .

SUMM . . . esters of the carboxylic acids salicylic acid, acetic acid, olycolic acid, palmitic acid and the like. Other non-limiting examples of **vitamin B.sub.3** compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methyl-nicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde,

isonicotinic acid,. . .

SUMM Examples of the above **vitamin B.sub.** **3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM One or more **vitamin B.sub.3** compounds may be used herein. Preferred **vitamin B.sub.3** compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

SUMM . . . and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating **skin** condition described herein.

SUMM Salts of the vitamin B3 compound are also useful herein. Nonlimiting examples of salts of the **vitamin B.sub.** **3** compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide,. . .

SUMM In a preferred embodiment, the ring nitrogen of the **vitamin B.sub.3** compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the **skin** becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the **vitamin B.sub.3** compound is essentially uncomplexed. Therefore, if the composition contains the **vitamin B.sub.3** compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the **skin**. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility. . .

SUMM More preferably the **vitamin B.sub.** **3** compound is substantially uncomplexed in the composition prior to delivery to the **skin**. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the **vitamin B.sub.3** compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the **vitamin B.sub.** **3** compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill. . .

SUMM Thus, in a preferred embodiment, the **vitamin B.sub.** **3** compound contains a limited amount of the salt form and is more preferably substantially free of salts of a **vitamin B.sub.3** compound. Preferably the **vitamin B.sub.3** compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The **vitamin B.sub.3** compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about. . .

SUMM The **vitamin B.sub.3** compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The **vitamin B.sub.** **3** compound is preferably substantially pure, more preferably essentially pure.

SUMM (ii) Retinoids: In a preferred embodiment, the compositions of the present invention contain a retinoid. The retinoid enhances the **skin** appearance benefits of the present invention, especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores.

SUMM As used herein, "retinoid" includes all natural and/or synthetic analogs

of **Vitamin A** or retinol-like compounds which possess the biological activity of **Vitamin A** in the **skin** as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably retinol, retinol esters (e.g., C.sub.2 -C.sub.22 alkyl esters of retinol, including retinyl **palmitate**, retinyl acetate, retinyl propionate), retinal, and/or retinoic acid (including all-trans retinoic acid and/or 13-cis-retinoic acid), more preferably retinoids other than. . . adapalene {6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid}, and tazarotene (ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)-ethynyl]nicotinate). One or more retinoids may be used herein. Preferred retinoids are retinol, retinyl **palmitate**, retinyl acetate, retinyl proprionate, retinal and combinations thereof. More preferred are retinol and retinyl **palmitate**.

SUMM . . . contain a safe and effective amount of the retinoid, such that the resultant composition is safe and effective for regulating **skin** condition, preferably for regulating visible and/or tactile discontinuities in **skin**, more preferably for regulating signs of **skin** aging, even more preferably for regulating visible and/or tactile discontinuities in **skin** texture associated with **skin** aging. The compositions preferably contain from or about 0.005% to or about 2%, more preferably 0.01% to or about 2%,. . .

SUMM In a preferred embodiment, the composition contains both a retinoid and a **Vitamin B.sub.3** compound. The retinoid is preferably used in the above amounts, and the **vitamin B.sub.3** compound is preferably used in an amount of from or about 0. 1% to or about 10%, more preferably from. . .

SUMM . . . which can cause increased scaling or texture changes in the stratum corneum and against other environmental agents which can cause **skin** damage.

SUMM Anti-oxidants/radical scavengers such as ascorbic acid (**vitamin C**) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate), tocopherol (**vitamin E**), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under. . . acid and its salts, lycine pidolate, arginine pilolate, nordihydroguaiaretic acid, bioflavonoids, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape **skin**/seed extracts, melanin, and rosemary extracts may be used. Preferred anti-oxidants/radical scavengers are selected from tocopherol sorbate and other esters of. . .

SUMM . . . about 5%, also preferably from about 0.5% to about 2%. Salicylic acid is preferred. The organic hydroxy acids enhance the **skin** appearance benefits of the present invention. For example, the organic hydroxy acids tend to improve the texture of the **skin**.

SUMM 3. Water soluble **skin** conditioning component: Preferred compositions of the invention can also comprise a water soluble **skin** conditioning component comprising one or more water soluble **skin** conditioning compounds. The water soluble **skin** conditioning component is useful for lubricating the **skin**, increasing the smoothness and suppleness of the **skin**, preventing or relieving dryness of the **skin**, hydrating the **skin**, and/or protecting the **skin**. The **skin** conditioning component enhances the **skin** appearance improvements of the present invention, including but not limited to essentially immediate visual improvements in **skin** appearance. The water soluble **skin** conditioning component is preferably selected from the group consisting of humectants, moisturizers and mixtures thereof. The water soluble **skin** conditioning

component is preferably present at a level of at least about 0.1%, more preferably from about 1% to about. . .

SUMM . . . 0.1% to about 10%, more preferably from about 0.5% to about 5%, of the composition. The anti-inflammatory agent enhances the **skin** appearance benefits of the present invention, e.g., such agents contribute to a more uniform and acceptable **skin** tone or color. The exact amount of anti-inflammatory agent to be used in the compositions will depend on the particular. . .

SUMM An agent may also be added to any of the compositions useful in the subject invention to improve the **skin** substantivity of those compositions, particularly to enhance their resistance to being washed off by water, or rubbed off. A preferred. . .

SUMM . . . of a chelating agent is especially useful for providing protection against UV radiation which can contribute to excessive scaling or **skin** texture changes and against other environmental agents which can cause **skin** damage.

SUMM . . . about 0.2% to about 5%, also preferably from about 0.5% to about 4% of the composition. Desquamation agents enhance the **skin** appearance benefits of the present invention. For example, the desquamation agents tend to improve the texture of the **skin** (e.g., smoothness). A variety of desquamation agents are known in the art and are suitable for use herein, including but. . .

SUMM 9. **Skin** Lightening Agents: The compositions of the present invention may comprise a **skin** lightening agent. When used, the compositions preferably comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%, of a **skin** lightening agent. Suitable **skin** lightening agents include those known in the art, including kojic acid, arbutin, ascorbic acid and derivatives thereof, e.g., magnesium ascorbyl phosphate. **Skin** lightening agents suitable for use herein also include those described in copending patent application Ser. No. 08/479,935, filed on Jun.. . .

SUMM . . . Preferred rinse-off cleansing compositions, such as shampoos, include a delivery system adequate to deposit sufficient levels of actives on the **skin** and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure of such delivery. . .

SUMM As used herein, the term "foundation" refers to a liquid, semi-liquid, or semi-solid **skin** cosmetic which includes, but is not limited to lotions, creams, gels, pastes, and the like. Typically the foundation is used over a large area of the **skin**, such as over the face, to provide a particular look. Foundations are typically used to provide an adherent base for color cosmetics such as rouge, blusher, and the like, and tend to hide **skin** imperfections and impart a smooth, even appearance to the **skin**. Foundations of the present invention include a dermatologically acceptable carrier for the essential particulate material and may include conventional ingredients. . .

SUMM VII Methods for Regulating **Skin** Condition

SUMM The compositions of the present invention are useful for regulating mammalian **skin** condition (especially human **skin**, more especially human facial **skin**), including regulating visible and/or tactile discontinuities in **skin**, e.g., visible and/or tactile discontinuities in **skin** texture, more especially discontinuities associated with **skin** aging.

SUMM A wide range of quantities of the compositions of the present invention can be employed to provide a **skin** appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm.sup.2 **skin**, from about 0.1 mg/cm.sup.2 to about 10 mg/cm.sup.2. A particularly useful application amount is about 2 mg/cm.sup.2. Typically applications would. . .

SUMM The compositions of this invention provide a visible improvement in **skin** condition essentially immediately following application of the composition to the **skin**. Such immediate improvement involves coverage or masking of **skin** imperfections such as textural discontinuities (including those associated with **skin** aging, such as enlarged pores), and/or providing a more even **skin** tone or color.

SUMM In a preferred embodiment, the composition includes an active which chronically regulates **skin** condition and is topically applied chronically. "Chronic topical application" and the like involves continued topical application of the composition over. . . preferably for at least about six months, and more preferably still for at least about one year. Chronic regulation of **skin** condition involves improvement of **skin** condition following multiple topical applications of the composition to the **skin**. While benefits are obtainable after various maximum periods of use (e.g., five, ten or twenty years), it is preferred that. . . however application rates can vary from about once per week up to about three times per day or more. Regulating **skin** condition involves topically applying to the **skin** a safe and effective amount of a composition of the present invention. The amount of the composition which is applied,. . . the active levels of a given composition and the level of regulation desired, e.g., in light of the level of **skin** aging present in the subject and the rate of further **skin** aging.

SUMM Regulating **skin** condition is preferably practiced by applying a composition in the form of a **skin** lotion, cream, cosmetic, or the like which is intended to be left on the **skin** until **skin** cleansing is appropriate, for some esthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition). After applying the composition to the **skin**, it is preferably left on the **skin** for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at. . .

DETD . . . 0.72

0.72

Stearyl Alcohol

0.48 0.48

0.48

0.48

PEG-100 Stearate

0.10 0.10

0.10

0.10

Stearic Acid 0.10 0.10

0.10

0.10

Vitamin E Acetate

-- 0.50

0.50

--

Butylated Hydroxy Toluene

0.001 -- -- 0.001

Phase C:

NaOH 0.30 0.25

0.25

0.25

Phase D:

Water. . . 0.10 0.10

0.10

0.10

NaCl 0.02

Phase F:

Dimethicone (and)

	2.00	2.00		
		2.00		
			2.00	
Dimethiconol				
Phase G				
Retinol	0.05	--	--	0.05
Vitamin E Acetate	0.50	--	--	0.50

.sup.1 A C1-C30 monoester or polyester of sugars and one or more carboxylic acid moieties. . .

DETD Applying each composition obtained from Examples 1-3 to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** to provides an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

DETD . . .	0.72	0.72		
Stearyl Alcohol	0.48	0.48	0.48	0.48
PEG-100 Stearate	0.10	0.10	--	0.10
Stearic Acid	0.10	0.10	--	0.10
Vitamin E Acetate	0.50	0.50	--	--
Steareth-21	--	--	0.56	--
Steareth-2	--	--	0.06	--
Phase NaOH	0.25	0.25	0.25	0.25

C:

Phase. . .

DETD . . . are prepared in the manner described for Examples 1-3. Apply each composition obtained from Examples 5-7 to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** to provide an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

DETD Application to the **skin** of the compositions obtained from Examples 8 and 9 to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** provides an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

DETD Apply the composition obtained from Example 10 to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** to provide an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

CLM What is claimed is:

1. A **skin** care composition which upon topical application to **skin** provides immediate visual improvement of **skin** appearance, which composition is in the form of an oil-in-water or water-in-oil emulsion, and which composition comprises: (A) a . hydrophilic. . . hyaluronate, ammonium hyaluronate, sodium algenate, ammonium alegenate, ammonium laurate, sodium laurate, potassium laurate, ammonium myristate, sodium myristate, potassium myristate, ammonium **palmitate**, sodium **palmitate**, potassium **palmitate**, ammonium stearate, sodium stearate, potassium stearate, ammonium oleate, sodium oleate, potassium oleate, and mixtures thereof; and (B) from about 1%. . .

2. A method of manufacturing a topical, aesthetically pleasing composition for providing **skin** conditioning and immediate visual improvement of **skin** appearance, comprising the steps of (A) mixing together, in any sequence, (1) from about 1% to about 98%, by weight. . . hyaluronate, ammonium hyaluronate, sodium algenate, ammonium algenate, ammonium laurate, sodium laurate, potassium laurate, ammonium myristate, sodium myristate, potassium myristate, ammonium **palmitate**, sodium **palmitate**, potassium **palmitate**, ammonium stearate, sodium stearate, potassium stearate, ammonium oleate, sodium oleate, potassium oleate, and mixtures thereof; and (B) adjusting the pH. . .

. . . 1 wherein the composition further comprises one or more compounds selected from the group consisting of emulsifiers, surfactants, structuring agents, **skin** care actives, and combinations thereof.

. . . of from about 1 to about 8 and a melting point of at least about 45.degree. C.; and (C) said **skin** care active is selected from the group consisting of **vitamin B.sub.** **3** compounds, retinoids, anti-oxidants, and mixtures thereof.

. . . surfactant; from about 1% to about 20% of the structuring agent; and from about 0.0001% to about 20% of the **skin** care active.

14. A composition according to claim 10 wherein said one or more **skin** care active is selected from the group consisting of niacinamide, retinol, retinal, retinyl **palmitate**, retinyl propionate, ascorbic acid, tocopherol, and derivatives and mixtures thereof.

17. A method of regulating **skin** condition comprising topically applying the composition of claim 1.

18. The method according to claim 17 wherein regulating **skin** condition comprises masking imperfections on the **skin** surface.

L7 ANSWER 5 OF 18 USPATFULL
AN 1999:155678 USPATFULL
TI Therapeutic system for dietary health management
IN Khoo, Chor San Heng, Mt. Laurel, NJ, United States
MacNair, R. David, King of Prussia, PA, United States
PA Campbell Soup Company, Camden, NJ, United States (U.S. corporation)
PI US 5994295 19991130 <--
AI US 1997-927076 19970910 (8)
RLI Continuation of Ser. No. US 1995-466893, filed on 6 Jun 1995, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Baker & Botts, LLP

CLMN Number of Claims: 52
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 3239
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5994295 19991130 <--
SUMM The NCI also suggests that diets rich in foods containing **Vitamin C** and **Vitamin A** from fruits and vegetables may also reduce the risk of cancer. Epidemiologic studies have shown that diets high in **Vitamin A** and **Vitamin C** are associated with lower risks of some kinds of cancers. Therefore, the NCI recommends consumption of a variety of fruits and vegetables, including fruit and vegetable juices that are high in **Vitamin A** and **Vitamin C**. Especially beneficial are cruciferous vegetables which are good sources of fiber, as well as vitamins and minerals.
DETD . . . major sources of dietary fat rather than by eliminating whole categories of foods. For example, by substituting fish, poultry without **skin**, lean meats and low- or non-fat dairy products for high-fat foods, a patient may lower total fat and SFA intake. . .
DETD TABLE I

Nutrient	Daily Desired Level of Fortification: Breakfast Meal (35%)	Lunch Meal (30%)	Dinner Meal (35%)
VITAMIN A, (IU)	1750	1500	1750
VITAMIN D, (IU)	140	120	140
VITAMIN E, (IU)	10.5	9	10.5
VITAMIN C, (mg)	35	30	35
VITAMIN B.sub.1, (mg)	0.53	0.45	0.53
VITAMIN B.sub.2, (mg)	0.6	0.51	0.6
VITAMIN B.sub.3, (mg)	7	6	7
VITAMIN B.sub.6, (mg)	0.7	0.6	0.7
VITAMIN B.sub.12, (mcg)	2.1	1.8	2.1
BIOTIN, (mcg)	105	90. . .	

DETD TABLE III

NUTRIENT	U.S. Recommended Dietary Allowance USRDA) USRDA
VITAMIN A	5000 IU
VITAMIN B.sub.1	1.5 mg
VITAMIN B.sub.2	1.7 mg
VITAMIN B.sub.3	20 mg NE.sup.1
VITAMIN B.sub.6	2 mg
VITAMIN B.sub.12	6 mcg
VITAMIN C	60 mg
VITAMIN D	400 IU
VITAMIN E	30 IU
VITAMIN K	NONE ESTABLISHED
BIOTIN	300 mcg
CALCIUM	1000 mg
COPPER	2 mg
FOLIC ACID	400 mcg
IODINE. . .	

DETD TABLE IV

DFEA Compositions

NUTRIENT	CONCENTRATION RANGE
VITAMIN A	1125-9900 IU
VITAMIN B.sub.1	0.41-2.07 mg
VITAMIN B.sub.2	0.23-2.24 mg
VITAMIN B.sub.3	6.3-25.3 mg NE
VITAMIN B.sub.6	0.54-2.75 mg
VITAMIN B.sub.12	1.08-8.58 mcg
VITAMIN C	31.5-330 mg
VITAMIN D	36-682 IU
VITAMIN E	9.45-49.5 IU
VITAMIN K	0-110 mcg
BIOTIN	94.5-412.5 mcg
CALCIUM	108-1333.2 mg
COPPER	0.95-3.63 mg
FOLIC ACID	126-660 mcg
IODINE. . .	

DETD TABLE VIII

Vitamin and Mineral Mixture (Frozen Foods)

NUTRIENT	CONCENTRATION	FORM
VITAMIN A	9000 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	1.88 mg	Thiamine Mononitrate
VITAMIN B.sub.2	2.04 mg	Riboflavin
VITAMIN B.sub.3	23 mg NE	Niacinamide
VITAMIN B.sub.6	2.5 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	7.8 mcg	Vitamin B.sub.12
VITAMIN C	300 mg	Ascorbic Acid
VITAMIN D	620 IU	Vitamin D.sub.3
VITAMIN E	45 IU	**Vitamin E** Acetate
VITAMIN K	100 mcg	Vitamin K.sub.1
BIOTIN	375 mcg	Biotin
CALCIUM	1212 mg	Calcium Citrate/ Dicalcium Phosphate
COPPER	3.3. . .	

DETD . . . humidity, e.g. in a range of about 35 to 75% RH, to produce a homogenous vitamin mix: 36 mg of **Vitamin A Palmitate** (250 micron spray dried); 300 mg of Ascorbic Acid; 6.2 mg of Vitamin D.sub.3 -100 S.D.; 90 mg of **Vitamin E** acetate 50% (CWS/F); 10 mg of Vitamin K.sub.1, 1% (spray dried); 1.88 mg of Thiamine Mononitrate; 2.04 mg of Riboflavin;. . .

DETD TABLE IX

Vitamin and Mineral Mixture (Cereals)

NUTRIENT	CONCENTRATION	FORM
VITAMIN A	2500 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	0.59 mg	Thiamine Mononitrate
VITAMIN B.sub.2	0.32 mg	Riboflavin
VITAMIN B.sub.3	7.7 mg NE	Niacinamide
VITAMIN B.sub.6	0.84 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	2.4 mcg	Vitamin B.sub.12
VITAMIN C	140 mg	Ascorbic Acid/Sodium Ascorbate
VITAMIN D	80 IU	Vitamin D.sub.3

VITAMIN E 15.75 IU **Vitamin E** Acetate
BIOTIN 141.75 mcg Biotin
CALCIUM 123.6 mg Calcium Carbonate
COPPER 1.16 mg Copper Gluconate
FOLIC ACID 210 mcg Folic. . .
DETD TABLE X

Vitamin and Mineral Mixture (Soups and Other Retorted Meals)

NUTRIENT	CONCENTRATION	FORM
VITAMIN A	9000 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	2.63 mg	Thiamine Mononitrate
VITAMIN B.sub.2	2.04 mg	Riboflavin
VITAMIN B.sub.3	23 mg	NE Niacinamide
VITAMIN B.sub.6	2.5 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	7.8 mcg	Vitamin B.sub.12
VITAMIN C	300 mg	Ascorbic Acid
VITAMIN D	620 IU	Vitamin D.sub.3
VITAMIN E	45 IU	**Vitamin E** Acetate
VITAMIN K	100 mcg	Vitamin K.sub.1
BIOTIN	375 mcg	Biotin
CALCIUM	1212 mg	Calcium Citrate/ Dicalcium Phosphate
COPPER	3.3. . .	

DETD TABLE XI

Garlic Roll

Nutrient	Fortification Level
VITAMIN A, (IU)	2250
VITAMIN D, (IU)	155
VITAMIN E, (IU)	11.25
VITAMIN C, (mg)	75
VITAMIN B.sub.1, (mg)	0.47
VITAMIN B.sub.2, (mg)	0.51
VITAMIN B.sub.3, (mg NE)	5.75
VITAMIN B.sub.6, (mg)	0.63
VITAMIN B.sub.12, (mcg)	1.95
BIOTIN, (mcg)	93.75
FOLIC ACID, (mcg)	150
PANTOTHNIC ACID,. . .	

DETD TABLE XII

Raisin Bran Cereal

Nutrient	Fortification Level
VITAMIN A, (IU)	2500
VITAMIN D, (IU)	80
VITAMIN E, (IU)	15.75
VITAMIN C, (mg)	140
VITAMIN B.sub.1, (mg)	0.59
VITAMIN B.sub.2, (mg)	0.32
VITAMIN B.sub.3, (mg NE)	7.7
VITAMIN B.sub.6, (mg)	0.84
VITAMIN B.sub.12, (mcg)	2.4
BIOTIN, (mcg)	141.75
FOLIC ACID, (mcg)	210
PANTOTHENIC ACID,. . .	

DETD TABLE XIII

Apple Crisp

Nutrient Level	Fortification
VITAMIN A, (IU)	1620
VITAMIN D, (IU)	111.6
VITAMIN E, (IU)	8.1
VITAMIN C, (mg)	54
VITAMIN B.sub.1, (mg)	0.34
VITAMIN B.sub.2, (mg)	0.37
VITAMIN B.sub.3, (mg NE)	4.14
VITAMIN B.sub.6, (mg)	0.45
VITAMIN B.sub.12, (mcg)	1.4
BIOTIN, (mcg)	67.5
FOLIC ACID, (mcg)	108
PANTOTHENIC ACID,. . .	

DETD TABLE XIV

Whipped Potatoes

Nutrient Level	Fortification
VITAMIN A, (IU)	1080
VITAMIN D, (IU)	74.4
VITAMIN E, (IU)	5.4
VITAMIN C, (mg)	36
VITAMIN B.sub.1, (mg)	0.23
VITAMIN B.sub.2, (mg)	0.25
VITAMIN B.sub.3, (mg NE)	2.76
VITAMIN B.sub.6, (mg)	0.3
VITAMIN B.sub.12, (mcg)	0.94
BIOTIN, (mcg)	45
FOLIC ACID, (mcg)	72
PANTOTHENIC ACID,. . .	

DETD TABLE XV

Orange Juice Drink

Nutrient Level	Fortification
VITAMIN A, (IU)	1800
VITAMIN D, (IU)	124
VITAMIN E, (IU)	9
VITAMIN C, (mg)	60
VITAMIN B.sub.1, (mg)	0.38
VITAMIN B.sub.2, (mg)	0.41
VITAMIN B.sub.3, (mg NE)	4.6
VITAMIN B.sub.6, (mg)	0.5
VITAMIN B.sub.12, (mcg)	1.56
BIOTIN, (mcg)	75
FOLIC ACID, (mcg)	120
PANTOTHENIC ACID,. . .	

DETD TABLE XVI

Vegetable Soup

Nutrient Level	Fortification
VITAMIN A, (IU)	2700
VITAMIN D, (IU)	186

VITAMIN E, (IU) 13.5
VITAMIN C, (mg) 90
VITAMIN B.sub.1, (mg) 0.79
VITAMIN B.sub.2, (mg) 0.61
VITAMIN B.sub.3, (mg NE) 6.9
VITAMIN B.sub.6, (mg) 0.75
VITAMIN B.sub.12, (mcg) 2.34
BIOTIN, (mcg) 112.1
FOLIC ACID, (mcg) 180
PANTOTHENIC ACID,. . .

DETD TABLE XVII

Fruit Sauce

Nutrient Level	Fortification
VITAMIN A, (IU)	450
VITAMIN D, (IU)	31
VITAMIN E, (IU)	2.25
VITAMIN C, (mg)	15
VITAMIN B.sub.1, (mg)	0.09
VITAMIN B.sub.2, (mg)	0.1
VITAMIN B.sub.3, (mg NE)	1.15
VITAMIN B.sub.6, (mg)	0.13
VITAMIN B.sub.12, (mcg)	0.39
BIOTIN, (mcg)	18.75
FOLIC ACID, (mcg)	30
PANTOTHENIC ACID,.	. .

DETD TABLE XVIII

Bagel

Nutrient Level	Fortification
VITAMIN A, (IU)	450
VITAMIN D, (IU)	31
VITAMIN E, (IU)	2.25
VITAMIN C, (mg)	15
VITAMIN B.sub.1, (mg)	0.09
VITAMIN B.sub.2, (mg)	0.1
VITAMIN B.sub.3, (mg NE)	1.15
VITAMIN B.sub.6, (mg)	0.13
VITAMIN B.sub.12, (mcg)	0.39
BIOTIN, (mcg)	18.75
FOLIC ACID, (mcg)	30
PANTOTHENIC ACID,.	. .

DETD TABLE XIX

Salisbury Steak

Nutrient Level	Fortification
VITAMIN A, (IU)	2700
VITAMIN D, (IU)	186
VITAMIN E, (IU)	13.5
VITAMIN C, (mg)	90
VITAMIN B.sub.1, (mg)	0.54
VITAMIN B.sub.2, (mg)	0.61
VITAMIN B.sub.3, (mg NE)	6.9
VITAMIN B.sub.6, (mg)	0.75
VITAMIN B.sub.12, (mcg)	2.34
BIOTIN, (mcg)	112.1

FOLIC ACID, (mcg) 180
PANTOTHENIC ACID,. . .
DETD TABLE XX

Salisbury Steak Gravy
. Fortification
Nutrient Level

VITAMIN A, (IU) 450
VITAMIN D, (IU) 31
VITAMIN E, (IU) 2.25
VITAMIN C, (mg) 15
VITAMIN B.sub.1, (mg) 0.09
VITAMIN B.sub.2, (mg) 0.1
VITAMIN B.sub.3, (mg NE) 1.15
VITAMIN B.sub.6, (mg) 0.13
VITAMIN B.sub.12, (mcg) 0.39
BIOTIN, (mcg) 18.75
FOLIC ACID, (mcg) 30
PANTOTHENIC ACID,. . .
DETD . . . 6
(g)
Sugar (g) 18 33 35 23
Protein (g) 21 14 16 13
PERCENTAGE OF U.S. RECOMMENDED DIETARY
ALLOWANCES (USRDA)
Vitamin A 35 35 35 35
Vitamin C 55 55 55 55
Calcium 40 40 40 40
Iron 35 35 35 35
Vitamin D 35 35 35 35
Vitamin E 35 35 35 35
Thiamine 35 35 35 35
Riboflavin 35 35 35 35
Niacin 35 35 35 35
Vitamin. . .
DETD . . . Fiber (g)
Sugar (g) 9 11 15 11
Protein (g) 19 26 20 20
PERCENTAGE OF U.S. RECOMMENDED DIETARY
ALLOWANCES (USRDA)
Vitamin A 30 30 30 30
Vitamin C 50 50 50 50
Calcium 35 35 35 35
Iron 30 30 30 30
Vitamin D 30 30 30 30
Vitamin E 30 30 30 30
Thiamine 30 30 30 30
Riboflavin 30 30 30 30
Niacin 30 30 30 30
Vitamin. . .
DETD . . . 8
Sugar (g) 7 8 6 13 18
Protein (g) 26 24 31 27 33
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES
(USRDA)
Vitamin A 35 35 35 35 35
Vitamin C 55 55 55 55 55
Calcium 40 40 40 40 40
Iron 35 35 35 35 35
Vitamin D 35 35 35 35 35
Vitamin E 35 35 35 35 35

Thiamine 35 35 35 35 35
Riboflavin 35 35 35 35 35
Niacin 35 35. . . 9
Sugar (g) 12 10 11 19 15
Protein (g) 27 28 32 29 25
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)
Vitamin A 35 35 35 35 35
Vitamin C 55 55 55 55 55
Calcium 40 40 40 40 40
Iron 35 35 35 35 35
Vitamin D 35 35 35 35 35
Vitamin E 35 35 35 35 35
Thiamine 35 35 35 35 35
Riboflavin 35 35 35 35 35
Niacin 35 35. . .
DETD . . . 3 2
Sugar (g) 2 1 9 11
Protein (g) 6 5 11 10
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)
Vitamin A 4 4 4 4
Vitamin C 4 4 & 4
Calcium 4 4 4 4
Iron 4 4 4 4
Vitamin D 4 4 4 4
Vitamin E 4 4 4 4
Thiamine 4 4 4 4
Riboflavin 4 4 4 4
Niacin 4 4 4 4
Vitamin. . .
DETD . . . life. The trial was also to monitor the safety of the Prepared Diet by monitoring nutritional intake in plasma vitamins (**Vitamin A** and Vitamin D) and mineral (iron), and trace minerals levels.

L7 ANSWER 6 OF 18 USPATFULL
AN 1999:137208 USPATFULL
TI Therapeutic system for dietary health management
IN Khoo, Chor San Heng, Mt. Laurel, NJ, United States
MacNair, R. David C., King of Prussia, PA, United States
PA Campbell Soup Company, Camden, NJ, United States (U.S. corporation)
PI US 5977059 19991102 <--
AI US 1997-926432 19970910 (8)
RLI Division of Ser. No. US 1995-466893, filed on 6 Jun 1995, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Baker & Botts, LLP
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 3081
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5977059 19991102 <--
SUMM The NCI also suggests that diets rich in foods containing **Vitamin C** and **Vitamin A** from fruits and vegetables may also reduce the risk of cancer. Epidemiologic studies have shown that diets high in **Vitamin A** and **Vitamin C** are associated with lower risks of some kinds of cancers. Therefore, the NCI recommends consumption of a variety of fruits and vegetables, including fruit and vegetable juices that are

high in **Vitamin A** and **Vitamin C**.
Especially beneficial are cruciferous vegetables which are good sources of fiber, as well as vitamins and minerals.

DETD . . . major sources of dietary fat rather than by eliminating whole categories of foods. For example, by substituting fish, poultry without **skin**, lean meats and low- or non-fat dairy products for high-fat foods, a patient may lower total fat and SFA intake. . .

DETD TABLE I

Daily Desired Level of Fortification	Breakfast Meal	Lunch Meal	Dinner Meal
Nutrient	(35%)	(30%)	(35%)
VITAMIN A, (IU)	1750	1500	1750
VITAMIN D, (IU)	140	120	140
VITAMIN E, (IU)	10.5	9	10.5
VITAMIN C, (mg)	35	30	35
VITAMIN B.sub.1, (mg)	0.53	0.45	0.53
VITAMIN B.sub.2, (mg)	0.6	0.51	0.6
VITAMIN B.sub.3, (mg)	7	6	7
VITAMIN B6, (mg)	0.7	0.6.	0.7
VITAMIN B.sub.12, (mcg)	2.1	1.8	2.1
BIOTIN, (mcg)	105	90.	. .

DETD TABLE III

U.S. Recommended Dietary Allowance (USRDA)

NUTRIENT	USRDA
VITAMIN A	5000 IU
VITAMIN B.sub.1	1.5 mg
VITAMIN B.sub.2	1.7 mg
VITAMIN B.sub.3	20 mg NE.sup.1
VITAMIN B.sub.6	2 mg
VITAMIN B.sub.12	6 mcg
VITAMIN C	60 mg
VITAMIN D	400 IU
VITAMIN E	30 IU
VITAMIN K	NONE ESTABLISHED
BIOTIN	300 mcg
CALCIUM	1000 mg
COPPER	2 mg
FOLIC ACID	400 mcg
IODINE. . .	

DETD TABLE IV

DFEA Compositions

NUTRIENT RANGE	CONCENTRATION
VITAMIN A	1125-9900 IU
VITAMIN B.sub.1	0.41-2.07 mg
VITAMIN B.sub.2	0.23-2.24 mg
VITAMIN B.sub.3	6.3-25.3 mg NE
VITAMIN B.sub.6	0.54-2.75 mg
VITAMIN B.sub.12	1.08-8.58 mcg
VITAMIN C	31.5-330 mg
VITAMIN D	36-682 IU
VITAMIN E	9.45-49.5 IU
VITAMIN K	0-110 mcg

BIOTIN 94.5-412.5 mcg
CALCIUM 108-1333.2 mg
COPPER 0.95-3.63 mg
FOLIC ACID 126-660 mcg
IODINE. . .

DETD TABLE VIII

Vitamin and Mineral Mixture (Frozen Foods)

NUTRIENT	CONCEN-TRATION	FORM
VITAMIN A	9000 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	1.88 mg	Thiamine Mononitrate
VITAMIN B.sub.2	2.04 mg	Riboflavin
VITAMIN B.sub.3	23 mg	NE Niacinamide
VITAMIN B.sub.6	2.5 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	7.8 mcg	Vitamin B12
VITAMIN C	300 mg	Ascorbic Acid
VITAMIN D	620 IU	Vitamin D.sub.3
VITAMIN E	45 IU	Vitainin E Acetate
VITAMIN K	100 mcg	Vitamin K.sub.1
BIOTIN	375 mcg	Biotin
CALCIUM	1212 mg	Calcium Citrate/Dicalcium

. . .

DETD . . . humidity, e.g. in a range of about 35 to 75% RH, to produce a homogenous vitamin mix: 36 mg of **Vitamin A Palmitate** (250 micron spray dried); 300 mg of Ascorbic Acid; 6.2 mg of Vitamin D.sub.3 --100 S.D.; 90 mg of **Vitamin E** acetate 50% (CWS/F); 10 mg of Vitamin K.sub.1, 1% (spray dried); 1.88 mg of Thiamine Mononitrate; 2.04 mg of Riboflavin;. . .

DETD TABLE IX

Vitmnin and Mineral Mixture (Cereals)

NUTRIENT	CON-CENTRATION	FORM
VITAMIN A	2500 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	0.59 mg	Thiamine Mononitrate
VITAMIN B.sub.2	0.32 mg	Riboflavin
VITAMIN B.sub.3	7.7 mg	NE Niacinamide
VITAMIN B.sub.6	0.84 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	2.4 mcg	Vitamin B.sub.12
VITAMIN C	140 mg	Ascorbic Acid/Sodium Ascorbate
VITAMIN D	80 IU	Vitamin D.sub.3
VITAMIN E	15.75 IU	**Vitamin E** Acetate
BIOTIN	141.75 mcg	Biotin
CALCIUM	123.6 mg	Calcium Carbonate
COPPER	1.16 mg	Copper Gluconate
FOLIC ACID	210 mcg	Folic. . .

DETD TABLE X

Vitamin and Mineral Mixture (Soups and Other Retorted Meals)

NUTRIENT	CON-CENTRATION	FORM
VITAMIN A	9000 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	2.63 mg	Thiamine Mononitrate
VITAMIN B.sub.2	2.04 mg	Riboflavin

VITAMIN B.sub.3 23 mg NE Niacinamide
VITAMIN B.sub.6 2.5 mg Pyridoxine Hydrochloride
VITAMIN B.sub.12 7.8 mcg Vitamin B.sub.12
VITAMIN C 300 mg Ascorbic Acid
VITAMIN D 620 IU Vitamin D.sub.3
VITAMIN E 45 IU **Vitamin E** Acetate
VITAMIN K 100 mcg Vitamin K.sub.1
BIOTIN 375 mcg Biotin
CALCIUM 1212 mg Calcium Citrate/Dicalcium Phosphate
COPPER 3.3 mg. . .

DETD TABLE XI

Garlic Roll

Nutrient Level	Fortification
VITAMIN A, (IU)	2250
VITAMIN D, (IU)	155
VITAMIN E, (IU)	11.25
VITAMIN C, (mg)	75
VITAMIN B.sub.1, (mg)	0.47
VITAMIN B.sub.2, (mg)	0.51
VITAMIN B.sub.3, (mg NE)	5.75
VITAMIN B.sub.6, (mg)	0.63
VITAMIN B.sub.12, (mcg)	1.95
BIOTIN, (mcg)	93.75
FOLIC ACID, (mcg)	150
PANTOTHENIC ACID,. . .	

DETD TABLE XII

Raisin Bran Cereal

Nutrient Level	Fortification
VITAMIN A, (IU)	2500
VITAMIN D, (IU)	80
VITAMIN E, (IU)	15.75
VITAMIN C, (mg)	140
VITAMIN B.sub.1, (mg)	0.59
VITAMIN B.sub.2, (mg)	0.32
VITAMIN B.sub.3, (mg NE)	7.7
VITAMIN B.sub.6, (mg)	0.84
VITAMIN B.sub.12, (mcg)	2.4
BIOTIN, (mcg)	141.75
FOLIC ACID, (mcg)	210
PANTOTHENIC ACID,. . .	

DETD TABLE XIII

Apple Crisp

Nutrient Level	Fortification
VITAMIN A, (IU)	1620
VITAMIN D, (IU)	111.6
VITAMIN E, (IU)	8.1
VITAMIN C, (mg)	54
VITAMIN B.sub.1, (mg)	0.34
VITAMIN B.sub.2, (mg)	0.37
VITAMIN B.sub.3, (mg NE)	4.14
VITAMIN B.sub.6, (mg)	0.45
VITAMIN B.sub.12, (mcg)	1.4

BIOTIN, (mcg) 67.5
FOLIC ACID, (mcg) 108
PANTOTHENIC ACID,. . .
DETD TABLE XIV

Whipped Potatoes

Nutrient Level	Fortification
VITAMIN A, (IU)	1080
VITAMIN D, (IU)	74.4
VITAMIN E, (IU)	5.4
VITAMIN C, (mg)	36
VITAMIN B.sub.1, (mg)	0.23
VITAMIN B.sub.2, (mg)	0.25
VITAMIN B.sub.3, (mg NE)	2.76
VITAMIN B.sub.6, (mg)	0.3
VITAMIN B.sub.12, (mcg)	0.94
BIOTIN, (mcg)	45
FOLIC ACID, (mcg)	72
PANTOTHENIC ACID,. . .	

DETD TABLE XV

Orange Juice Drink

Nutrient Level	Fortification
VITAMIN A, (IU)	1800
VITAMIN D, (IU)	124
VITAMIN E, (IU)	9
VITAMIN C, (mg)	60
VITAMIN B.sub.1, (mg)	0.38
VITAMIN B.sub.2, (mg)	0.41
VITAMIN B.sub.3, (mg NE)	4.6
VITAMIN B.sub.6, (mg)	0.5
VITAMIN B.sub.12, (mcg)	1.56
BIOTIN, (mcg)	75
FOLIC ACID, (mcg)	120
PANTOTHENIC ACID,. . .	

DETD TABLE XVI

Vegetable Soup

Nutrient Level	Fortification
VITAMIN A, (IU)	2700
VITAMIN D, (IU)	186
VITAMIN E, (IU)	13.5
VITAMIN C, (mg)	90
VITAMIN B.sub.1, (mg)	0.79
VITAMIN B.sub.2, (mg)	0.61
VITAMIN B.sub.3, (mg NE)	6.9
VITAMIN B.sub.6, (mg)	0.75
VITAMIN B.sub.12, (mcg)	2.34
BIOTIN, (mcg)	112.1
FOLIC ACID, (mcg)	180
PANTOTHENIC ACID,. . .	

DETD TABLE XVII

Fruit Sauce

Nutrient Level	Fortification

VITAMIN A, (IU) 450
VITAMIN D, (IU) 31
VITAMIN E, (IU) 2.25
VITAMIN C, (mg) 15
VITAMIN B.sub.1, (mg) 0.09
VITAMIN B.sub.2, (mg) 0.1
VITAMIN B.sub.3, (mg NE) 1.15
VITAMIN B.sub.6, (mg) 0.13
VITAMIN B.sub.12, (mcg) 0.39
BIOTIN, (mcg) 18.75
FOLIC ACID, (mcg) 30
PANTOTHENIC ACID,. . .
DETD TABLE XVIII

Bagel

Fortification
Nutrient Level

VITAMIN A, (IU) 450
VITAMIN D, (IU) 31
VITAMIN E, (IU) 2.25
VITAMIN C, (mg) 15
VITAMIN B.sub.1, (mg) 0.09
VITAMIN B.sub.2, (mg) 0.1
VITAMIN B.sub.3, (mg NE) 1.15
VITAMIN B.sub.6, (mg) 0.13
VITAMIN B.sub.12, (mcg) 0.39
BIOTIN, (mcg) 18.75
FOLIC ACID, (mcg) 30
PANTOTHENIC ACID,. . .
DETD TABLE XIX

Salisbury Steak

Fortification
Nutrient Level

VITAMIN A, (IU) 2700
VITAMIN D, (IU) 186
VITAMIN E, (IU) 13.5
VITAMIN C, (mg) 90
VITAMIN B.sub.1, (mg) 0.54
VITAMIN B.sub.2, (mg) 0.61
VITAMIN B.sub.3, (mg NE) 6.9
VITAMIN B.sub.6, (mg) 0.75
VITAMIN B.sub.12, (mcg) 2.34
BIOTIN, (mcg) 112.1
FOLIC ACID, (mcg) 180
PANTOTHENIC ACID,. . .
DETD TABLE XX

Salisbury Steak Gravy

Fortification
Nutrient Level

VITAMIN A, (IU) 450
VITAMIN D, (IU) 31
VITAMIN E, (IU) 2.25
VITAMIN C, (mg) 15
VITAMIN B.sub.1, (mg) 0.09
VITAMIN B.sub.2, (mg) 0.1
VITAMIN B.sub.3, (mg NE) 1.15

VITAMIN B.sub.6, (mg) 0.13
VITAMIN B.sub.12, (mcg) 0.39
BIOTIN, (mcg) 18.75
FOLIC ACID, (mcg) 30
PANTOTHENIC ACID,. . .
DETD . . . 7 7 6
Sugar (g) 18 33 35 23
Protein (g) 21 14 16 13
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)
Vitamin A 35 35 35 35
Vitamin C 55 55 55 55
Calcium 40 40 40 40
Iron 35 35 35 35
Vitamin D 35 35 35 35
Vitamin E 35 35 35 35
Thiamine 35 35 35 35
Riboflavin 35 35 35 35
Niacin 35 35 35 35
Vitamin. . .
DETD . . . 5 7
Sugar (g) 9 11 15 11
Protein (g) 19 26 20 20
PERCENTAGE OF U.S. RECOMMENDED
DIETARY ALLOWANCES (USRDA)
Vitamin A 30 30 30 30
Vitamin C 50 50 50 50
Calcium 35 35 35 35
Iron 30 30 30 30
Vitamin D 30 30 30 30
Vitamin E 30 30 30 30
Thiamine 30 30 30 30
Riboflavin 30 30 30 30
Niacin 30 30 30 30
Vitamin. . .
DETD . . . 27 33

PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)

	GRILLED BBQ CHICKEN	GRILLED MUSTARD CHICKEN	HERB ROASTED CHICKEN	POT MEATLOAF	ROAST

Vitamin A 35 35 35 35 35
Vitamin C 55 55 55 55 55
Calcium 40 40 40 40 40
Iron 35 35 35 35 35
Vitamin D 35 35 35 35 35
Vitamin E 35 35 35 35 35
Thiamine 35 35 35 35 35
Riboflavin 35 35 35 35 35
Niacin 35 35. . . 9
Sugar (g) 12 10 11 19 15
Protein (g) 27 28 32 29 25
PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)
Vitamin A 35 35 35 35 35
Vitamin C 55 55 55 55 55
Calcium 40 40 40 40 40
Iron 35 35 35 35 35
Vitamin D 35 35 35 35 35
Vitamin E 35 35 35 35 35
Thiamine 35 35 35 35 35

Riboflavin 35 35 35 35 35
Niacin 35 35. . .
DETD . . . 3 2
Sugar (g) 2 1 9 11
Protein (g) 6 5 11 10
PERCENTAGE OF U.S. RECOMMENDED
DIETARY ALLOWANCES (USRDA)
Vitamin A 4 4 4 4
Vitamin C 4 4 4 4
Calcium 4 4 4 4
Iron 4 4 4 4
Vitamin D 4 4 4 4
Vitamin E 4 4 4 4
Thiamine 4 4 4 4
Riboflavin 4 4 4 4
Niacin 4 4 4 4
Vitamin. . .
DETD . . . life. The trial was also to monitor the safety of the Prepared Diet by monitoring nutritional intake in plasma vitamins (**Vitamin A** and Vitamin D) and mineral (iron), and trace minerals levels.

L7 ANSWER 7 OF 18 USPATFULL
AN 1999:136663 USPATFULL
TI UV protection compositions
IN Robinson, Larry Richard, Loveland, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5976513 19991102 <--
AI US 1999-264139 19990305 (9)
RLI Continuation-in-part of Ser. No. US 1998-174225, filed on 16 Oct 1998, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dodson, Shelley A.
LREP Kendall, Dara M., Henderson, Loretta J., Hilton, Michael E.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 906
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5976513 19991102 <--
SUMM It is well known that exposure to sunlight can pose a number of hazards to the **skin**. These damaging effects may result not only from sunbathing but also from the sunlight exposure associated with daily outdoor activities.. . . a wavelength of from about 290 nm to about 320 nm. Over the long term, however, malignant changes in the **skin** surface often occur. Numerous epideminologic studies demonstrate a strong relationship between sunlight exposure and human **skin** cancer. Another long term hazard of ultraviolet radiation is premature aging of the **skin**, which is primarily caused by UVA radiation having a wavelength of from about 320 nm to about 400 nm. This condition is characterized by wrinkling and pigment changes of the **skin**, along with other physical changes such as cracking, telangiectasis, solar dermatoses, ecchymoses, and loss of elasticity. The adverse effects associated. . .
SUMM . . . care products" refer to health and cosmetic beauty aid products generally recognized as being formulated for beautifying and grooming the **skin** and hair. For example, personal care products include sunscreen products (e.g., lotions, **skin** creams, etc.), cosmetics, toiletries, and over-the-counter pharmaceutical products intended for topical usage.

SUMM . . . are efficient at absorbing UV radiation in the 290 nm to 320 nm UVB region such that sunburn of the **skin** is prevented. They are less efficient when it comes to absorbing light which falls in the 320 nm to 400 nm UVA region, which leaves the **skin** vulnerable to premature **skin** aging. This deficiency is due in part to the limited number of UVA absorbing sunscreen actives which are both commercially. . .

SUMM . . . there is a need for photostabilized compositions suitable for providing protection against the harmful effects of UV radiation to human **skin**. In particular, in the personal care industry, a need remains for sunscreen products having excellent photostability, efficiency, and which provide. . .

SUMM . . . and most preferably from about 2:1 to about 1:1. The present invention also relates to methods for providing protection to **skin** from the harmful effects of UV radiation by topical application of such compositions. Furthermore, the present invention relates to methods. . .

SUMM . . . compositions of the present invention are useful for providing protection against the harmful effects of ultraviolet radiation, especially to human **skin**. The essential components of these compositions are described below. Also included is a nonexclusive description of various optional and preferred. . .

SUMM . . . against erythema. The SPF is defined as the ratio of the ultraviolet energy required to produce minimal erythema on protected **skin** to that required to produce the same minimal erythema on unprotected **skin** in the same individual. See Federal Register, 43, No. 166, pp. 38206-38269, Aug. 25, 1978).

SUMM . . . use application. For example, carriers of the present invention include, but are not limited to, those suitable for application to **skin**, hair, nails, animal **skin**, fur, automobiles, fabrics, marine vehicles, as well as those suitable for incorporation into plastics, metals, etc.. Preferably, the carriers of the present invention are suitable for application to **skin** (e.g., sunscreens, creams, milks, lotions, masks, serums, etc.); hair and fur (e.g., shampoos, hair setting or treatment gels or lotions,. . . lacquers or lotions, etc,); and nails (e.g., polishes, treatments, etc.). In preferred embodiments, the carrier is suitable for application to **skin** which means that the carrier and its components are suitable for use in contact with **skin**, hair, fur, and nails without undue toxicity, incompatibility, instability, allergic response, and the like within the scope of sound medical. . . and can include one or more compatible liquid or solid filler diluents or vehicles which are suitable for application to **skin**, hair, fur, and nails. The exact amount of carrier will depend upon the level of the UVA-absorbing dibenzoylmethane sunscreen active,. . .

SUMM . . . etc.), hair care and styling products (e.g., shampoos, conditioners, gels, mousses, sprays, etc.), topical animal care items (e.g., shampoos, conditioners, **skin** treatments, etc.). Any additional components required to formulate such products vary with product type and can be routinely chosen by. . .

SUMM If compositions of the present invention are formulated as an aerosol and applied to the **skin** as a spray-on product, a propellant is added to the composition. Examples of suitable propellants include chlorofluorinated lower molecular weight. . .

SUMM In a preferred embodiment, where the composition is to be in contact with human **skin**, the optional components should be suitable for application to **skin**, that is, when incorporated into the composition they are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability, allergic response, and the like within the scope of sound medical judgment. The CTFA Cosmetic Ingredient Handbook, Second Edition (1992) describes a wide variety of nonlimiting cosmetic and pharmaceutical ingredients commonly

used in the **skin** care industry, which are suitable for use in the compositions of the present invention. Examples of these ingredient classes include: abrasives, absorbents, aesthetic components such as fragrances, pigments, colorings/colorants, essential oils, **skin** sensates, astringents, etc. (e.g., clove oil, menthol, camphor, eucalyptus oil, eugenol, menthyl lactate, witch hazel distillate), anti-acne agents, anti-caking agents,. . . and substantivity of the composition (e.g., copolymer of eicosene and vinyl pyrrolidone), opacifying agents, pH adjusters, propellants, reducing agents, sequestrants, **skin** bleaching and lightening agents (e.g., hydroquinone, kojic acid, ascorbic acid, magnesium ascorbyl phosphate, ascorbyl glucosamine), **skin**-conditioning agents (e.g., humectants, including miscellaneous and occlusive), **skin** soothing and/or healing agents (e.g., panthenol and derivatives (e.g., ethyl panthenol), aloe vera, pantothenic acid and its derivatives, allantoin, bisabolol, and dipotassium glycyrrhizinate), **skin** treating agents, thickeners, and vitamins and derivatives thereof.

SUMM . . . such optional components. Preferred compositions optionally contain one or more materials selected from UVB sunscreen actives, anti-acne actives, vitamin compounds, **skin** treating agents, humectants, moisturizers, **skin** conditioners, thickening agents, structuring agents, and emulsifiers.

SUMM . . . These vitamin compounds may be in either natural or synthetic form. Suitable vitamin compounds include, but are not limited to, **Vitamin A** (e.g., beta carotene, retinoic acid, retinol, retinoids, retinyl **palmitate**, retinyl proprionate, etc.), Vitamin B (e.g., niacin, niacinamide, riboflavin, pantothenic acid, etc.), **Vitamin C** (e.g., ascorbic acid, etc.), Vitamin D (e.g., ergosterol, ergocalciferol, cholecalciferol, etc.), **Vitamin E** (e.g., tocopherol acetate, etc.), and Vitamin K (e.g., phytonadione, menadione, phthiocol, etc.) compounds.

SUMM In particular, the compositions of the present invention may comprise a safe and effective amount of a **vitamin B.sub .3** compound. **Vitamin B.sub. 3** compounds are particularly useful for regulating **skin** condition as described in co-pending U.S. application Ser. No. 08/834,010, filed Apr. 11, 1997 (corresponding to international publication WO 97/39733. . . and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the **vitamin B.sub.3** compound.

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR7## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B. sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM Examples of suitable **vitamin B.sub. 3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM d) **Skin** Treating Agent

SUMM The compositions of the present invention may contain one or more **skin** treating agents. Suitable **skin** treating agents include those effective for preventing, retarding, arresting, and/or reversing **skin** wrinkles. Examples of suitable **skin** treating agents include, but are not limited to, alpha-hydroxy acids such as lactic acid and glycolic acid and beta-hydroxy acids. . .

SUMM g) Humectants, Moisturizers, and **Skin** Conditioners

SUMM Preferred compositions optionally comprise one or more humectants, moisturizers, or **skin** conditioners. A variety of these materials can be employed and each can be present at a level of from

about. . .
SUMM . . . products. More preferably, the compositions of the present invention are suitable for use as sunscreens to provide protection to human **skin** from the harmful effects of UV radiation which include, but are not limited to, sunburn and premature aging of the **skin**. The present invention therefore also further relates to methods of protecting human **skin** from the harmful effects of UV radiation. Such methods generally involve attenuating or reducing the amount of UV radiation which reaches the **skin**'s surface. To protect the **skin** from UV radiation, a safe and effective (photoprotective) amount of the composition is topically applied to the **skin**. "Topical application" refers to application of the present compositions by spreading, spraying, etc. onto the surface of the **skin**. The exact amount applied may vary depending on the level of UV protection desired. From about 0.5 mg of composition per cm.sup.2 of **skin** to about 25 mg of composition per cm.sup.2 of **skin** are typically applied.
DETD . . . DEA Oleth-3 Phosphate 0.75 0.75 0.75 0.75
Stearic Acid 1.00 1.00 1.00 1.00
Cetyl Alcohol 1.00 1.00 1.00 1.00
Cetyl **Palmitate** 0.50 0.50 0.50 0.50
Triethanolamine 0.70 0.70 1.5 1.5

.sup.1 Available as Pemulen TR1 from B. F. Goodrich
DETD . . . the octyl methoxycinnamate, octyl salicylate, isopropyl myristate, propyl paraben, 1-acetonaphthone, 1-naphthaldehyde, 4-t-butyl-4'-methoxydibenzoylmethane, DEA oleth-3-phosphate, stearic acid, cetyl alcohol, and cetyl **palmitate** in a separate vessel with mixing and heating to 75.degree. C. Next, mix the oil phase into the water phase. . .
CLM What is claimed is:
18. A method for providing protection against the harmful effects of ultraviolet radiation to **skin**, said method comprising applying a safe and effective amount of the composition of claim 1 to **skin**.

L7 ANSWER 8 OF 18 USPATFULL
AN 1999:132881 USPATFULL
TI Pharmaceutical compositions and methods for improving wrinkles and other **skin** conditions
IN Murad, Howard, 4316 Marina City Dr., Marina del Rey, CA, United States 90292
PI US 5972999 19991026 <--
AI US 1998-146554 19980903 (9)
RLI Continuation of Ser. No. US 1997-787358, filed on 22 Jan 1997, now patented, Pat. No. US 5804594
DT Utility
FS Granted
EXNAM Primary Examiner: MacMillan, Keith D.
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1077
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Pharmaceutical compositions and methods for improving wrinkles and other **skin** conditions
PI US 5972999 19991026 <--
AB This application relates to a pharmaceutical composition for the prevention and treatment of **skin** conditions in a patient having a sugar compound that is converted to a glycosaminoglycan in the

patient in an amount sufficient to thicken the **skin**, a primary antioxidant component in an amount sufficient to substantially inhibit the formation of collagenase and elastase, at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**, and at least one transition metal component in an amount effective to bind collagen and elastic fibers and rebuild **skin** . In one preferred form, the composition further includes a catechin-based preparation, a glucosamine or a pharmaceutically acceptable salt or ester. . . a chondroitin or a pharmaceutically acceptable salt or ester thereof. In a more preferred form, the invention further includes a **vitamin E** source, a cysteine source, a **vitamin B.sub.3** source, quercetin dihydrate, pyridoxal 5 phosphate-Co B.sub.6, a methionine source, and a **vitamin A** source. The invention further relates to a method for the prevention or treatment of **skin** conditions by administering the pharmaceutical composition in an amount therapeutically effective to modify the thickness of the **skin** to prevent or treat at least one **skin** condition.

SUMM . . . well as methods, to supplement collagen and elastic tissues and thicken the dermis for the treatment of wrinkles and other **skin** conditions.

SUMM Human **skin** is a composite material of the epidermis and the dermis. The topmost part of the epidermis is the stratum corneum. This layer is the stiffest layer of the **skin**, as well as the one most affected by the surrounding environment. Below the stratum corneum is the internal portion of. . . the dermis is the papillary dermis, which is made of relatively loose connective tissues that define the micro-relief of the **skin**. The reticular dermis, disposed beneath the papillary dermis, is tight, connective tissue that is spatially organized. The reticular dermis is. . .

SUMM The principal functions of the **skin** include protection, excretion, secretion, absorption, thermoregulation, pigmentogenesis, accumulation, sensory perception, and regulation of immunological processes. These functions are detrimentally affected by the structural changes in the **skin** due to aging and excessive sun exposure. The physiological changes associated with **skin** aging include impairment of the barrier function and decreased turnover of epidermal cells, for example. [Cerimele, D., et al., Br.. . .

SUMM The mechanical properties of the **skin**, such as elasticity, are controlled by the density and geometry of the network of collagen and elastic fiber tissue therein. Damaged collagen and elastin lose their contractile properties, resulting in **skin** wrinkling and **skin** surface roughness. As the **skin** ages or becomes unhealthy, it acquires sags, stretch marks, bumps, bruises or wrinkles, it roughens, and it has reduced ability to synthesize Vitamin D. Aged **skin** also becomes thinner and has a flattened dermoepidermal interface because of the alterations in collagen, elastin, and glycosaminoglycans. [Fenske, N.. . .

SUMM A variety of vitamins and minerals have in individually been administered to treat certain **skin** and other problems that occur when the patient has a deficiency of that vitamin or mineral. **Vitamin A**, for example, assists in the treatment of acne and to facilitate wound healing; **vitamin C** (ascorbic acid) assists in the prevention of **skin** bruising and wound healing; **vitamin E** is an antioxidant; and copper assists in the treatment of elastic tissue defects. [Neldner, K. H., Amer. Acad. Derm. Annl. Mtg., Wash. D.C., Dec. 6, 1993]. Topical use of **vitamin C** is also believed to ward off sun damage, reduce breakdown of connective tissues, and possibly promote collagen synthesis. [Dial, W., Medical World News, p. 12, March 1991]. **Vitamin E** is used topically as an anti-inflammatory agent, for enhancement of **skin** moisturization, for UV-ray

protection of cells, and for retardation of premature **skin** aging.

SUMM . . . metabolism of glycosaminoglycans under the influence of herbal and other anti-inflammatory agents has been examined by measuring glycosaminoglycans in the **skin**, liver, kidney, and spleen after administration of several compounds. [Reddy, G. K., et al., Biochem. Pharmacology, 38(20) :3527-3534 (1989)].

SUMM . . . a patient, various of the above ingredients have been combined to form pharmaceuticals designed to prevent and treat certain cellular, **skin**, and other conditions. For example, U.S. Pat. No. 3,773,930 discloses a low residue, dietary composition having at least one amino. . .

SUMM U.S. Pat. No. 4,414,202 discloses a composition for the treatment of **skin** wounds with a buffered salt solution having a pH between 6 to 7.8 and administering a starch hydrolysate compound, and. . .

SUMM U.S. Pat. No. 4,424,232 discloses a topical composition for the treatment of herpes simplex, cold sores, lesions, and other painful **skin** conditions including L-lysine, gibberellic acid, and urea in an inert carrier having water. The composition may also include L-ascorbic acid,. . .

SUMM U.S. Pat. No. 5,198,465 discloses a composition for treating precursor deficiencies in the synthesis of collagen with proline, glycine, lysine, **vitamin C**, and one or more compounds selected from .alpha.-ketoglutaric acid, methionine, cysteine, cystine, valine, and pharmaceutically acceptable diluents and excipients.

SUMM . . . complexes; an enzyme producer such as an amino acid like glutamic acid; an herbal antispasmodic substance like Valerian root; and **vitamin C**.

SUMM U.S. Pat. No. 5,415,875 discloses a method of suppressing formation of lipid peroxide and removing peroxide by applying to the **skin** a decomposed product of shell membrane and tocopherol and derivatives. Lysine, proline, **Vitamin C**, for examples, are listed among a vast genus of optional additives.

SUMM The above references, however, do not teach pharmaceutical compositions or methods for improving **skin** wrinkles along with other conditions, such as **skin** elasticity and softness. Thus, it is desired to find a pharmaceutical composition and a method for the prevention and treatment of wrinkles and other **skin** conditions. The present invention advantageously provides pharmaceutical compositions, as well as methods of treatment comprising the administration of such compositions, to repair **skin** for the prevention and treatment of wrinkles and other **skin** disorders.

SUMM The present invention relates to a pharmaceutical composition for the prevention and treatment of **skin** conditions in a patient having a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**, a primary antioxidant component in an amount sufficient to substantially inhibit the activity of collagenase and elastase, at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**, and at least one transition metal component in an amount effective to bind collagen and elastic fibers and rebuild **skin** .

SUMM In another preferred embodiment, the composition further includes a **vitamin E** source, a cysteine source, a **vitamin B.sub.3** source, quercetin dihydrate, pyridoxal 5 phosphate-Co B.sub.6, a methionine source, and a **vitamin A** source. In a more preferred embodiment, the **vitamin E** is D-alpha tocopheryl acid succinate present in about 1 to 15 weight percent, the **vitamin B. sub.3** is niacinamide present in about 0.5 to 15 weight percent, the **vitamin A** is **vitamin A palmitate** present in about 0.1 to 5 weight percent,

the cysteine is N-acetyl cysteine present in about 1 to 10 weight. . .

SUMM The invention further relates to a method for the prevention or treatment of **skin** conditions, wherein the **skin** has a thickness of dermis and collagen, which includes administering the pharmaceutical composition above in an amount therapeutically effective to modify the thickness of the **skin** to prevent or treat at least one **skin** condition.

SUMM In one embodiment according to the invention, the **skin** condition treated is at least one of wrinkles, fine lines, thinning, reduced **skin** elasticity, reduced **skin** moisture, spider veins, senile purpura, sun damaged **skin**, aging **skin**, or rough **skin**. In another embodiment, the composition is administered orally. In a preferred embodiment, the composition is administered as a tablet or. . .

SUMM . . . conjunction with concurrent or subsequent treatment by at least one additional pharmaceutical composition for the prevention or treatment of a **skin** condition.

SUMM A formulation for the reduction of wrinkles and the improvement of other **skin** conditions, such as increased **skin** elasticity and **skin** softness, has now been discovered. Moreover, the prevention or treatment of unhealthy **skin**, such as aged **skin** or **skin** overexposed to sunlight, may advantageously be accomplished by the administration of the pharmaceutical composition of the present invention to a. . . pharmaceutical composition includes the combination of a number of different components which interact to provide the desired improvements to the **skin**.

SUMM The advantageous pharmaceutical composition of the present invention prevents and improves **skin** conditions by using a sufficient amount of at least one sugar compound which is converted into glycosaminoglycans in the bloodstream,. . . supplementing collagen and elastic tissues. A thicker dermis desirably reduces the wrinkling and lines that occur when areas of the **skin** become thin. Various amino acids such as lysine, proline and cysteine assist in the thickening of the dermis, supplementing of collagen and elastic tissues and, consequently, reduction of wrinkles and other **skin** conditions. Additionally, antioxidants, such as **vitamin C**, inhibit collagenase and elastase, enzymes that break down collagen and elastic tissues. These antioxidants assist in the prevention of additional wrinkles and facilitate the healing of **skin** tissues. Finally, transition metal components are included to bind collagen fibers and inhibit elastase, an enzyme that also breaks down. . .

SUMM The pharmaceutical composition includes a primary antioxidant, which typically is a **vitamin C** source and preferably is ascorbic acid, or a pharmaceutically acceptable salt or ester thereof, and more preferably is ascorbyl **palmitate**, dipalmitate L-ascorbate, sodium L-ascorbate-2-sulfate, or an ascorbic salt, such as sodium, potassium, or calcium ascorbate, or mixtures thereof. When oral formulations of the pharmaceutical composition are used, it is preferred that a non-acidic form of **vitamin C** be used to reduce the stomach irritation that may occur when using an acidic form. The **vitamin C** source is present in the pharmaceutical composition in about 5 to 50 weight percent, preferably about 7 to 40 weight percent, and more preferably about 10 to 25 weight percent. A unit dose of this primary **vitamin C** source is typically about 40 mg to 400 mg, preferably about 60 mg to 300 mg, and more preferably about 80 to 150 mg. **Vitamin C** is also approved by the FDA and has wide consumer acceptance, so that it can be used in amounts as. . .

SUMM The pharmaceutical composition also includes at least one amino acid to assist in thickening the **skin**. Preferably two or more amino acids are used in combination. Either the L- or D- forms of amino acids

are. . .

SUMM . . . or more transition metal compounds are included in an amount effective to bind collagen and elastic tissue to rebuild the **skin**. Certain transition metal compounds inhibit the elastase enzyme to inhibit collagen and elastic tissue breakdown. Preferred transition metals include zinc,. . .

SUMM . . . assist in binding collagen and elastic fibers, which both assists in the prevention of wrinkles and the rebuilding of wrinkled **skin**. The zinc component may be any zinc compound or pharmaceutically acceptable salt thereof, but more preferably is a zinc complexed. . .

SUMM . . . or pharmaceutically acceptable salt thereof, but more preferably is a manganese component which is at least partially complexed with a **vitamin C** source, and most preferably is manganese ascorbate or manganese ascorbic acid, wherein the manganese is typically present in about 5 to 20 weight percent of the complex. When complexed with **vitamin C**, this **vitamin C** source may be included in the overall percentage of **vitamin C** in the pharmaceutical composition. The manganese component is present in about 1 to 10 weight percent, more preferably about 2. . .

SUMM The catechin-based preparation, similar to **vitamin C** , inhibits elastase and collagenase, which is another enzyme that attacks elastic tissue and collagen. The catechin-based preparation is preferably a. . .

SUMM . . . 90 weight percent of the salt. The glucosamine content of this component contributes to the formation of glycosoaminoglycans in the **skin**. The chondroitin component preferably is present as a sulfate or succinate, and more preferably is chondroitin sulfate, wherein the chondroitin. . .

SUMM In a more preferred form, several optional additives are included in the pharmaceutical composition, such as a **vitamin E** source, a **vitamin B.sub.3** source, quercetin powder, pyridoxal 5 phosphate-Co B.sub.6, and a **vitamin A** source. The **vitamin E** preferably is a sulfate or succinate **vitamin E** complex, and more preferably is D-alpha tocopheryl acid succinate. The **vitamin E** source is present in about 1 to 15 weight percent, preferably about 2 to 12 weight percent, and more preferably. . . 10 weight percent of the composition. In any event, no more than 1,500 IU should be ingested per day, as **Vitamin E** becomes toxic at higher doses. The **vitamin B. sub.3** source preferably is niacinamide, and the source is present in about 0.5 to 15 weight percent, preferably about 1 to 12 weight percent, and more preferably about 1.5 to 10 weight percent of the composition. The **vitamin A** source preferably is **vitamin A palmitate**, and the source is present in about 0.1 to 5 weight percent, preferably 0.2 to 3 weight percent, and more preferably 0.3 to 1 weight percent of the composition. In the more preferred form, the amount of **vitamin A** dosage is about 500,000 IU/gram per unit dose. **Vitamin A** is toxic at high levels, such that no more than 400,000 IU should be cumulatively ingested per day for greater. . .

SUMM . . . amount" means that amount of the pharmaceutical composition that provides a therapeutic benefit in the treatment, prevention, or management of **skin** wrinkles and other **skin** conditions.

DETD

Ingredient	Weight Percent (% w/w)	Amount (mg)	Chemical or Scientific Name (if different)

N-Acetylglucosamine			
	17.1	140	N-Acetyl D-Glucosamine
Vitamin C (81.2%			
	15	123.2	
Ascorbic Acid)			
L-Lysine (80%)			
	12.2	100	L-Lysine hydrochloride
L-Proline	11	90	
D-Glucosamine Sulfate			
	6.5	53.3	
(75%)			
Chondroitin Sulfate			
	6.1	50	
(80%)			
Vitamin E Succinate			
	4.3	39.7	D-.alpha. tocopheryl acid succinate
Zinc monomethionine			
	3.7	30	Zinc DL-methionine
(20%)			
N-Acetyl Cysteine			
	3.7	30	
Manganese Ascorbate			
	2.8	23.1	
(13% Mn)			
Vitamin B.sub.3			
	2.4	20	Niacinamide
Niacinamide			
Quercetin Powder			
	2.4	20	Quercetin dihydrate
Grape Seed Extract			
	0.9	7.5	Proanthocyanidin
Pyridoxal 5	0.6	5	P-5-P monohydrate
Phosphate-Co B.sub.6			
Selenomethionine			
	0.5	4	L-selenomethionine
(0.5%)			
Vitamin A Palmitate			
	0.5	4	
(500,000 IU/GR)			
Copper Sebacate (14%)			
	0.4	2.9	
Red beet root powder			
	6.1	50	Beta vulgaris rubra
Stearic acid	1.5	12	
Sorbitol	1.3	11	

Acdisol. . .

DETD . . . 73 female subjects to determine the effects on the elasticity, firmness, and presence of fine lines and wrinkles of the **skin**. A seven day conditioning period was used prior to initiation of the study, where subjects were instructed to discontinue use. . .

DETD The texture of the **skin**, fine lines, and wrinkles were assessed by taking Silflo replicas of the periorbital area (crow's feet) at each of the. . . replicas, were illuminated at a precisely defined angle of 35.degree. to create shadows for analysis by shades of gray. The **skin** topography is defined by the: (a) number of wrinkles; (b) total area of wrinkles; (c) total length of wrinkles; (d). . .

DETD . . . is a function of the length of treatment as indicated above.

This strongly suggests the treatment has imparted an improved **skin** infrastructure by beneficially affecting the dermis of the **skin**.

DETD The Ballistometer is an instrument designed to evaluate in vivo, in a non-invasive manner, the viscoelastic properties of the **skin**. It analyzes the bounce pattern displayed by a probe that is allowed to impact on the **skin**. The kinetic energy of the probe striking the **skin** is stored by the elastic components of the **skin** and released back to make the probe rebound to a lower height. The height to which the probe will rebound depends upon the amount of stored energy lost in shear viscosity within the **skin**.

DETD The capacity of the **skin** to absorb mechanical energy may thus be measured. Although it is unclear exactly which layer, or layers, of the **skin** are responsible, the mechanical properties of the dermis/epidermis layers are controlled by the density and geometry of the network of. . .

DETD . . . less of the energy of the striking probe was restored, thus, a greater amount of energy was dissipated in the **skin**. This suggests the **skin** became softer and more yielding during the test period.

DETD The Cutometer is a commercially available instrument (Courage & Khazaka, Germany) designed to measure the mechanical properties of the **skin** in a non-invasive manner. It measures the vertical deformation of the **skin**'s surface when pulled by vacuum suction (500 mm Hg) through the small aperture (2 mm) of a probe and the depth of penetration of the **skin** into the probe optically with an accuracy of 0.01 mm. The probe is attached to a computer, which completely controls probe operation and plots **skin** deformation as a function of time. From this curve, a number of variables can be extrapolated to estimate the elastic, viscoelastic, and purely viscous behavior of the **skin**.

DETD . . . final distension (U.sub.f), measured at 10 seconds; and (d) immediate retraction (U.sub.r). The deformation parameters are extrinsic parameters dependent on **skin** thickness, and a variety of biologically important ratios were calculated: (a) U.sub.r /U.sub.f, a measure of net elasticity of the **skin**; (b) U.sub.r /U.sub.e, the biological elasticity, or measurement of the ability of the **skin** to regain its initial configuration after deformation; and (c) U.sub.v /U.sub.e, the viscoelastic to elastic ratio, where an increase in. . .

DETD . . . distension (U.sub.v) decreased a significant 16 percent ($p<0.04$) after 5 weeks of treatment. This parameter reflects viscoelastic properties of the **skin** and, thus, the behavior of the dermis. After 5 weeks, there were no statistically significant changes in U.sub.e, the immediate. . .

DETD The general appearance of soft, smooth **skin** depends largely on the presence of an adequate amount of water in the stratum corneum. The Corneometer is a commercially available instrument (Courage & Khazaka, Germany) to measure the changes in capacitance of the **skin** resulting from changes in the degree of hydration. It is particularly sensitive to low levels of hydration, and uses measurements of arbitrary units of **skin** hydration (H) to express capacitance.

DETD . . . moisturizing agents and humectants. Thus, the measurements with the Ballistometer and Cutometer indicate changes occurred in deeper layers of the **skin**, rather than the superficial stratum corneum. Table IV shows no significant changes in the hydration of the stratum corneum following. . .

DETD TABLE IV

Corneometer Readings
Skin Hydration (H)

	Mid-Baseline		Final-Baseline	
	Control	Treated	Control	Treated
Average	-5	-7	-8	-4
Standard Deviation	6	7	5	7
p value	p <. . .			

CLM What is claimed is:

1. An orally administered pharmaceutical composition for the prevention and treatment of **skin** conditions in a patient comprising: a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**; a primary antioxidant component in an amount sufficient to substantially inhibit the activity of collagenase and elastase; at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**; and at least one transition metal component in an amount effective to bind collagen and elastic fibers and thicken **skin** .

7. The pharmaceutical composition of claim 1, further comprising a **vitamin E** source, a cysteine source, a **vitamin B.sub.3** source, quercetin dihydrate, pyridoxal 5 phosphate-Co B.sub.6, a methionine source, and a **vitamin A** source.

8. The pharmaceutical composition of claim 7, wherein the **vitamin E** is D-alpha tocopheryl acid succinate present in about 1 to 15 weight percent, the **vitamin B. sub.3** is niacinamide present in about 0.5 to 15 weight percent, the **vitamin A** is **vitamin A palmitate** present in about 0.1 to 5 weight percent, the cysteine is N-acetyl cysteine present in about 1 to 10 weight. . .

9. A method for the prevention or treatment of **skin** conditions, wherein the **skin** has a thickness of dermis and collagen, which comprises administering to a patient: a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**; a primary antioxidant component in an amount sufficient to substantially inhibit the activity of collagenase and elastase; at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**; and at least one transition metal component in an amount effective to bind collagen and elastic fibers and thicken **skin**, so as to modify the thickness of the **skin** to prevent or treat at least one **skin** condition.

10. The method of claim 9, wherein the **skin** condition prevented or treated is at least one of wrinkles or the appearance thereof, fine lines or the appearance thereof, thinning, reduced **skin** elasticity, reduced **skin** moisture, spider veins, senile purpura, sun damaged **skin**, aging **skin** or rough **skin**.

. . . conjunction with concurrent or subsequent treatment by at least one additional pharmaceutical composition for the prevention or treatment of a **skin** condition.

13. A method for the prevention or treatment of **skin** conditions, wherein the **skin** has a thickness of dermis and collagen, which comprises administering to a patient: a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**; a primary antioxidant

component in an amount sufficient to substantially inhibit the activity of collagenase and elastase; at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**; at least one transition metal component in an amount effective to bind collagen and elastic fibers and thicken **skin**; and a catechin-based component present in an amount sufficient to inhibit the presence of an anti-collagen enzyme in the **skin**, so as to modify the thickness of the **skin** to prevent or treat at least one **skin** condition.

14. An pharmaceutical composition for the prevention and treatment of **skin** conditions in a patient consisting essentially of: a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**; a primary antioxidant component in an amount sufficient to substantially inhibit the activity of collagenase and elastase; at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**; and at least one transition metal component in an amount effective to bind collagen and elastic fibers and thicken **skin**.

L7 ANSWER 9 OF 18 USPATFULL
AN 1999:132251 USPATFULL
TI **Skin** care compositions and method of improving **skin** appearance
IN Sine, Mark Richard, Cincinnati, OH, United States
SaNogueira, Jr., James Pedrosa, Cincinnati, OH, United States
Dawes, Nancy Coultrip, Cincinnati, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5972359 19991026 <--
AI US 1998-61509 19980417 (9)
RLI Continuation-in-part of Ser. No. US 1997-862775, filed on 23 May 1997, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dodson, Shelley A.
LREP Allen, George W., Matthews, Armina E., Henderson, Loretta J.
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2450
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI **Skin** care compositions and method of improving **skin** appearance
PI US 5972359 19991026 <--
AB Disclosed are topical compositions which provide good coverage of **skin** imperfections, e.g., pores and uneven **skin** tone, while retaining a natural **skin** appearance. The compositions contain a particulate material having a refractive index of at least about 2, e.g., TiO.sub.2.
SUMM The present invention relates to the field of topical compositions for improving the appearance or other condition of **skin**. More particularly, the invention relates to topical compositions which provide good coverage of **skin** imperfections, e.g., pores and uneven **skin** tone, while retaining a natural **skin** appearance.
SUMM . . . compounds have been described in the art as being useful for regulating fine lines, wrinkles and other forms of undesirable **skin** surface texture. In addition, **Vitamin B .sub.3** compounds, particularly niacinamide, have recently been found to provide measurable benefits in regulating **skin** condition, including regulating fine lines, wrinkles and

other forms of uneven or rough surface texture associated with aged or photodamaged **skin**. However, many materials require multiple applications over an extended period to provide such appearance benefits. It would be advantageous to. . . composition which provides a more immediate improvement in the appearance of fine lines, wrinkles, pores and other forms of undesirable **skin** surface texture.

SUMM Particulate materials, including TiO.sub.2, have been included in **skin** care compositions. For example, emulsions may contain TiO.sub.2 as an opacifying agent to provide a white appearance to the emulsion.. . . compositions may employ such particulates to impart a sunscreening effect. Several publications have also disclosed the use of TiO.sub.2 in **skin** care compositions. See, e.g., U.S. Pat. No. 5,223,559 and patent application Nos. DE 245815, WO 94/09756 and JP 08188723. In. . . the Soft-Focus Effect, Cosmetics & Toiletries, Vol. 111, July 1996, pp. 57-61). Emmert discloses that one can mechanically fill in **skin** lines with a reflective substance such as TiO.sub.2. However, Emmert teaches that such reflective materials result in an undesirable mask-like. . .

SUMM . . . as TiO.sub.2, of which the present inventors are aware, either do not provide coverage sufficient to reduce the appearance of **skin** imperfections, or tend to result in unacceptable **skin** whitening or other unnatural appearance when applied to the **skin**. It has also now been found that materials which primarily diffuse light, rather than reflect light, do not provide good coverage of **skin** imperfections when used in amounts which are esthetically acceptable to consumers. More particularly, when used at relatively high concentrations to provide coverage, these materials suffer from unacceptable **skin** whitening.

SUMM . . . have now found that reflective materials such as TiO.sub.2 can be formulated in topical compositions to provide good coverage of **skin** imperfections while retaining a generally natural appearance, e.g., without unacceptable **skin** whitening. The compositions are especially suitable for providing an immediate visual improvement in **skin** appearance.

SUMM . . . is an object of the present invention to provide topical compositions suitable for imparting an essentially immediate visual improvement in **skin** appearance. It is another object of the present invention to provide topical compositions containing a reflective particulate material, e.g., TiO.sub.2, which provide desirable coverage of **skin** imperfections such as pores and uneven **skin** tone, while maintaining a natural **skin** appearance (e.g., without unacceptable **skin** whitening). Another object of the present invention is to provide such topical compositions which are additionally useful for regulating **skin** appearance and/or condition, especially regulating textural or tonal discontinuities in **skin** (e.g., pores and uneven **skin** color).

SUMM The present invention also relates to methods of improving **skin** appearance and/or condition by topical application of the subject compositions.

SUMM . . . ZnO, and ZrO, with TiO.sub.2 being more preferred. The compositions are useful for imparting an essentially immediate visual improvement in **skin** appearance, while maintaining a natural **skin** appearance. Compositions of the invention are characterized by their contrast ratio and % transmittance or Coverage Index. Compositions of the. . .

SUMM . . . application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the **skin**.

SUMM . . . as used herein, means that the compositions or components thereof so described are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability,

allergic response, and the like.

SUMM . . . herein means an amount of a compound, component, or composition sufficient to significantly induce a positive benefit, preferably a positive **skin** appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to. . .

SUMM . . . compositions of the invention are useful for topical application and for providing an essentially immediate (i.e., acute) visual improvement in **skin** appearance following application of the composition to the **skin**. Without intending to be limited by theory, it is believed that this acute **skin** appearance improvement results at least in part from therapeutic coverage or masking of **skin** imperfections by the particulate material. The compositions provide the visual benefits without imparting an unacceptable **skin** appearance such as **skin** whitening.

SUMM More particularly, the compositions of the present invention are useful for regulating **skin** condition, including regulating visible and/or tactile discontinuities in **skin**, including but not limited to visible and/or tactile discontinuities in **skin** texture and/or color, more especially discontinuities associated with **skin** aging. Such discontinuities may be induced or caused by internal and/or external factors. Extrinsic factors include ultraviolet radiation (e.g., from. . . low humidity, harsh surfactants, abrasives, and the like. Intrinsic factors include chronological aging and other biochemical changes from within the **skin**.

SUMM Regulating **skin** condition includes prophylactically and/or therapeutically regulating **skin** condition. As used herein, prophylactically regulating **skin** condition includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in **skin**. As used herein, therapeutically regulating **skin** condition includes ameliorating, e.g., diminishing, minimizing and/or effacing, such discontinuities. Regulating **skin** condition involves improving **skin** appearance and/or feel, e.g., providing a smoother, more even appearance and/or feel. As used herein, regulating **skin** condition includes regulating signs of aging. "Regulating signs of **skin** aging" includes prophylactically regulating and/or therapeutically regulating one or more of such signs (similarly, regulating a given sign of **skin** aging, e.g., lines, wrinkles or pores, includes prophylactically regulating and/or therapeutically regulating that sign).

SUMM "Signs of **skin** aging" include, but are not limited to, all outward visibly and tactilely perceptible manifestations as well as any other macro or micro effects due to **skin** aging. Such signs may be induced or caused by intrinsic factors or extrinsic factors, e.g., chronological aging and/or environmental damage.. . . not limited to, the development of textural discontinuities such as wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, **skin** lines, crevices, bumps, large pores (e.g., associated with adnexal structures such as sweat gland ducts, sebaceous glands, or hair follicles), scaliness, flakiness and/or other forms of **skin** unevenness or roughness, loss of **skin** elasticity (loss and/or inactivation of functional **skin** elastin), sagging (including puffiness in the eye area and jowls), loss of **skin** firmness, loss of **skin** tightness, loss of **skin** recoil from deformation, discoloration (including undereye circles), blotching, sallowness, hyperpigmented **skin** regions such as age spots and freckles, keratoses, abnormal differentiation, hyperkeratinization, elastosis, collagen breakdown, and other histological changes in the stratum corneum, dermis, epidermis, the **skin** vascular system (e.g., telangiectasia or spider vessels), and underlying tissues, especially those proximate to the **skin**.

SUMM . . . to be understood that the present invention is not to be

limited to regulation of the above mentioned "signs of **skin** aging" which arise due to mechanisms associated with **skin** aging, but is intended to include regulation of said signs irrespective of the mechanism of origin. As used herein, "regulating **skin** condition" is intended to include regulation of such signs irrespective of the mechanism of origin.

SUMM The present invention is especially useful for therapeutically regulating visible and/or tactile discontinuities in mammalian **skin**, including discontinuities in **skin** texture and color. For example, the apparent diameter of pores decreases, the apparent height of tissue immediately proximate to pore openings approaches that of the interadnexal **skin**, the **skin** tone/color becomes more uniform, and/or the length, depth, and/or other dimension of lines and/or wrinkles are decreased.

SUMM . . . in essentially neat, powdered form or predispersed in various types of dispersants, including but not limited to isopropyl isostearate, isopropyl **palmitate**, methyl isostearate, Finsolv TN, cylcomethicone, and cyclomethicone and dimethicone copolyols.

SUMM . . . material and optional other materials are incorporated to enable the particulate material and optional components to be delivered to the **skin** at an appropriate concentration. The carrier can thus act as a diluent, dispersant, solvent, or the like for the particulate. . .

SUMM . . . Science and Technology 2nd Edition, Vol. 2, pp. 443-465 (1972), incorporated herein by reference. Aerosols are typically applied to the **skin** as a spray-on product.

SUMM . . . acceptable emollient. Such compositions preferably contain from about 2% to about 50% of the emollient. Emollients tend to lubricate the **skin**, increase the smoothness and suppleness of the **skin** , prevent or relieve dryness of the **skin**, and/or protect the **skin**. Emollients are typically water-immiscible, oily or waxy materials. A wide variety of suitable emollients are known and may be used. . .

SUMM . . . mousses. Toilet bars are most preferred since this is the form of cleansing agent most commonly used to wash the **skin**. Preferred rinse-off cleansing compositions, such as shampoos, include a delivery system adequate to deposit sufficient levels of actives on the **skin** and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure of such delivery. . .

SUMM As used herein, the term "foundation" refers to a liquid, semi-liquid, semi-solid, or solid **skin** cosmetic which includes, but is not limited to lotions, creams, gels, pastes, cakes, and the like. Typically the foundation is used over a large area of the **skin**, such as over the face, to provide a particular look. Foundations are typically used to provide an adherent base for color cosmetics such as rouge, blusher, powder and the like, and tend to hide **skin** imperfections and impart a smooth, even appearance to the **skin** . Foundations of the present invention include a dermatologically acceptable carrier for the essential particulate material and may include conventional ingredients. . .

SUMM . . . melting point of about 25.degree. C. or less under about one atmosphere of pressure, and are suitable for conditioning the **skin** or hair.

SUMM . . . acids include straight chain, branched chain and aryl carboxylic acids). Nonlimiting examples include diisopropyl sebacate, diisopropyl adipate, isopropyl myristate, isopropyl **palmitate**, methyl **palmitate**, myristyl propionate, 2-ethylhexyl **palmitate**, isodecyl neopentanoate, di-2-ethylhexyl maleate, cetyl **palmitate**, myristyl myristate, stearyl stearate, isopropyl stearate, methyl stearate, cetyl stearate, behenyl behenrate, dioctyl maleate, dioctyl sebacate, diisopropyl adipate, cetyl

octanoate,. . .

SUMM . . . cosmetic biocides, denaturants, cosmetic astringents, drug astringents, external analgesics, film formers, humectants, opacifying agents, fragrances, perfumes, pigments, colorings, essential oils, **skin** sensates, emollients, **skin** soothing agents, **skin** healing agents, pH adjusters, plasticizers, preservatives, preservative enhancers, propellants, reducing agents, **skin** -conditioning agents, **skin** penetration enhancing agents, **skin** protectants, solvents, suspending agents, emulsifiers, thickening agents, solubilizing agents, polymers for aiding the film-forming properties and substantivity of the composition. . . anti-androgens, depilation agents, desquamation agents/exfoliants, organic hydroxy acids, vitamins and derivatives thereof (including water dispersible or soluble vitamins such as **Vitamin C** and ascorbyl phosphates), compounds which stimulate collagen production, and natural extracts. Such other materials are known in the art. Nonexclusive. . .

SUMM In a preferred embodiment, the composition also includes an active useful for chronically regulating **skin** condition. Such materials are those which manifest **skin** appearance benefits following chronic application of the composition containing such materials. Materials having this effect include, but are not limited to, **Vitamin B.sub.3** compounds and retinoids.

SUMM A. **Vitamin B.sub.3** Compounds

SUMM In a preferred embodiment, the compositions of the present invention comprise a safe and effective amount of a **vitamin B. sub.3** compound. The **vitamin B. sub.3** compound enhances the **skin** appearance benefits of the present invention, especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores. The compositions of the present invention preferably comprise from about 0.01% to about. . .

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR3## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B. sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM . . . As used herein, "non-vasodilating" means that the ester does not commonly yield a visible flushing response after application to the **skin** in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds. . .

SUMM Other derivatives of the **vitamin B.sub. 3** compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of. . .

SUMM . . . esters of the carboxylic acids salicylic acid, acetic acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of **vitamin B.sub.3** compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methyl-nicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid,. . .

SUMM Examples of the above **vitamin B.sub. 3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM One or more **vitamin B.sub.3**

compounds may be used herein. Preferred **vitamin B.sub.3** compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

SUMM . . . and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating **skin** condition described herein.

SUMM Salts of the **vitamin B.sub.3** compound are also useful herein. Nonlimiting examples of salts of the **vitamin B.sub.3** compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide,. . . e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the **vitamin B.sub.3** compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic. . .

SUMM In a preferred embodiment, the ring nitrogen of the **vitamin B.sub.3** compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the **skin** becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the **vitamin B.sub.3** compound is essentially uncomplexed. Therefore, if the composition contains the **vitamin B.sub.3** compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the **skin**. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility. . .

SUMM More preferably the **vitamin B.sub.3** compound is substantially uncomplexed in the composition prior to delivery to the **skin**. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the **vitamin B.sub.3** compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the **vitamin B.sub.3** compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill. . .

SUMM Thus, in a preferred embodiment, the **vitamin B.sub.3** compound contains a limited amount of the salt form and is more preferably substantially free of salts of a **vitamin B.sub.3** compound. Preferably the **vitamin B.sub.3** compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The **vitamin B.sub.3** compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about. . .

SUMM The **vitamin B.sub.3** compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The **vitamin B.sub.3** compound is preferably substantially pure, more preferably essentially pure.

SUMM In a preferred embodiment, the compositions of the present invention contain a retinoid. The retinoid enhances the **skin** appearance benefits of the present invention, especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores.

SUMM As used herein, "retinoid" includes all natural and/or synthetic analogs

of **Vitamin A** or retinol-like compounds which possess the biological activity of **Vitamin A** in the **skin** as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably retinol, retinol esters (e.g., C.sub.2 -C.sub.22 alkyl esters of retinol, including retinyl **palmitate**, retinyl acetate, retinyl propionate), retinal, and/or retinoic acid (including all-trans retinoic acid and/or 13-cis-retinoic acid), more preferably retinoids other than. . . adapalene {6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid}, and tazarotene (ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)-ethynyl]nicotinate). One or more retinoids may be used herein. Preferred retinoids are retinol, retinyl **palmitate**, retinyl acetate, retinyl proprionate, retinal and combinations thereof. More preferred are retinol and retinyl **palmitate**.

SUMM . . . contain a safe and effective amount of the retinoid, such that the resultant composition is safe and effective for regulating **skin** condition, preferably for regulating visible and/or tactile discontinuities in **skin**, more preferably for regulating signs of **skin** aging, even more preferably for regulating visible and/or tactile discontinuities in **skin** texture associated with **skin** aging. The compositions preferably contain from or about 0.005% to or about 2%, more preferably 0.01% to or about 2%,. . .

SUMM In a preferred embodiment, the composition contains both a retinoid and a **Vitamin B.sub.3** compound. The retinoid is preferably used in the above amounts, and the **vitamin B.sub.3** compound is preferably used in an amount of from or about 0.1% to or about 10%, more preferably from or. . .

SUMM . . . 0.1% to about 10%, more preferably from about 0.5% to about 5%, of the composition. The anti-inflammatory agent enhances the **skin** appearance benefits of the present invention, e.g., such agents contribute to a more uniform and acceptable **skin** tone or color. The exact amount of anti-inflammatory agent to be used in the compositions will depend on the particular. . .

SUMM An agent may also be added to any of the compositions useful in the subject invention to improve the **skin** substantivity of those compositions, particularly to enhance their resistance to being washed off by water, or rubbed off. A preferred. . .

SUMM . . . which can cause increased scaling or texture changes in the stratum corneum and against other environmental agents which can cause **skin** damage.

SUMM Anti-oxidants/radical scavengers such as ascorbic acid (**vitamin C**) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate), tocopherol (**vitamin E**), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under. . . acid and its salts, lycine pidolate, arginine pilolate, nordihydroguaiaretic acid, bioflavonoids, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape **skin**/seed extracts, melanin, and rosemary extracts may be used. Preferred anti-oxidants/radical scavengers are selected from tocopherol sorbate and other esters of. . .

SUMM . . . of a chelating agent is especially useful for providing protection against UV radiation which can contribute to excessive scaling or **skin** texture changes and against other environmental agents which can cause **skin** damage.

SUMM . . . about 5%, also preferably from about 0.5% to about 2%. Salicylic acid is preferred. The organic hydroxy acids enhance the **skin** appearance benefits of the present invention. For example, the organic hydroxy acids tend to improve the texture of the **skin**.

SUMM . . . about 0.2% to about 5%, also preferably from about 0.5% to about 4% of the composition. Desquamation agents enhance the **skin** appearance benefits of the present invention. For example, the desquamation agents tend to improve the texture of the **skin** (e.g., smoothness). A variety of desquamation agents are known in the art and are suitable for use herein, including but. . .

SUMM I. **Skin** Lightening Agents

SUMM The compositions of the present invention may comprise a **skin** lightening agent. When used, the compositions preferably comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%, of a **skin** lightening agent. Suitable **skin** lightening agents include those known in the art, including kojic acid, arbutin, ascorbic acid and derivatives thereof, e.g., magnesium ascorbyl phosphate. **Skin** lightening agents suitable for use herein also include those described in copending patent application Ser. No. 08/479,935, filed on Jun.. . .

SUMM J. **Skin** Conditioners

SUMM Preferred compositions of the invention comprise an optional **skin** conditioning component comprising one or more **skin** conditioning compounds. The **skin** conditioning component is useful for lubricating the **skin**, increasing the smoothness and suppleness of the **skin**, preventing or relieving dryness of the **skin**, hydrating the **skin**, and/or protecting the **skin**. The **skin** conditioning component enhances the **skin** appearance improvements of the present invention, including but not limited to essentially immediate visual improvements in **skin** appearance. The **skin** conditioning component is preferably selected from the group consisting of emollients, humectants, moisturizers and mixtures thereof. The **skin** conditioning component is preferably present at a level of at least about 0.1%, more preferably from about 1% to about. . . and most preferably from about 5% to about 25% (e.g., about 5% to about 10% or 15%). Compositions containing the **skin** conditioning component tend to have the preferred Hydration Factors described herein.

SUMM . . . but are not limited to, methyl, isopropyl, and butyl esters of fatty acids such as hexyl laurate, isohexyl laurate, isohexyl **palmitate**, isopropyl **palmitate**, methyl **palmitate**, decyloleate, isodecyl oleate, hexadecyl stearate decyl stearate, isopropyl isostearate, methyl isostearate, diisopropyl adipate, diisohexyl adipate, dihexyldecyl adipate, diisopropyl sebacate, lauryl. . .

SUMM Preferred compositions of the present invention have a Hydration Factor of at least zero as measured by the **Skin** Moisturizer Hydration Test. The **Skin** Moisturizer Hydration Test evaluates and compares the in-vivo, hydration efficacy of topical compositions. The test method utilizes a Courage and Khazaka Comeometer 820 PC to measure the electrical capacitance of the **skin** surface. Without being limited by theory, it is believed that the electrical capacitance is an indirect measurement of water presence and therefore **skin** surface hydration.

SUMM The **Skin** Moisturizer Hydration Test is determined using at least 16 subjects in general good health (free of medical conditions, adverse reactions or sensitivities which might affect the **skin** test results). In general, the products to be tested are applied to the forearms of each subject, in an area. . .

SUMM Test Method: Apply the composition to the subject's **skin** as described above. Spread the composition on the test region by rubbing in a circular motion, using a cotted finger until the product has blended into the **skin** completely. Take electrical capacitance values with the corneometer at baseline (before product application) and then 3 hours, and 6 hours. . .

SUMM A comparatively higher corneometer reading indicates higher **skin** surface capacitance and therefore higher **skin** surface water content or hydration. The difference between the corneometer values of reference composition and the test formulation (which have. . .

SUMM Methods for Regulating **Skin** Condition

SUMM The compositions of the present invention are useful for regulating mammalian **skin** condition (especially human **skin**, more especially human facial **skin**), including regulating visible and/or tactile discontinuities in **skin**, e.g., visible and/or tactile discontinuities in **skin** texture, more especially discontinuities associated with **skin** aging.

SUMM A wide range of quantities of the compositions of the present invention can be employed to provide a **skin** appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm.sup.2 **skin**, from about 0.1 mg/cm.sup.2 to about 10 mg/cm.sup.2. A particularly useful application amount is about 2 mg/cm.sup.2. Typically applications would. . .

SUMM The compositions of this invention provide a visible improvement in **skin** condition essentially immediately following application of the composition to the **skin**. Such immediate improvement involves coverage or masking of **skin** imperfections such as textural discontinuities (including those associated with **skin** aging, such as enlarged pores), and/or providing a more even **skin** tone or color.

SUMM In a preferred embodiment, the composition includes an active which chronically regulates **skin** condition and is topically applied chronically. "Chronic topical application" and the like involves continued topical application of the composition over. . . preferably for at least about six months, and more preferably still for at least about one year. Chronic regulation of **skin** condition involves improvement of **skin** condition following multiple topical applications of the composition to the **skin**. While benefits are obtainable after various maximum periods of use (e.g., five, ten or twenty years), it is preferred that. . . however application rates can vary from about once per week up to about three times per day or more. Regulating **skin** condition involves topically applying to the **skin** a safe and effective amount of a composition of the present invention. The amount of the composition which is applied,. . . the active levels of a given composition and the level of regulation desired, e.g., in light of the level of **skin** aging present in the subject and the rate of further **skin** aging.

SUMM Regulating **skin** condition is preferably practiced by applying a composition in the form of a **skin** lotion, cream, cosmetic, or the like which is intended to be left on 5 the **skin** for an extended period, for some esthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition). As used herein, "leave-on" compositions exclude rinse-off **skin** cleansing products. After applying the composition to the **skin**, the leave-on composition is preferably left on the **skin** for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at. . .

DETD Apply the composition to a subjects facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** to provide an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even sldn tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

DETD . . . 6 6

TiO.sub.2 0.75 0.75

Phase C Glycerin 3 3
Carbopol 954 0.4 0.4
EDTA 0.1 0.1
Phase D Cetyl **Palmitate** 1.5 1.5
Cetyl Alcohol 2.25 2.25
Stearyl Alcohol 1.5 1.5
Stearic Acid 0.31 0.31
PEG-100 Stearate 0.31 0.31
Silicone Wax. . . distilled water 0 5
Phase G Glydant PIus 0.1 0.1
distilled water 1 1
glycerin 1 1
Phase H Isopropyl **Palmitate** 1.25 1.25
Retinol 0 0.04
Tween 80 0 0.04
BHT 0 0.05

DETD Apply the composition to a subject's facial **skin** at the rate of 2 mg composition/cm.sup.2 skln to provide an essentially immediate visual improvement in **skin** appearance, e.g., reduced visibility of pores and a more even **skin** tone. Apply the composition to a subject's face at the same rate once or twice daily for a period of 3-6 months, to improve **skin** surface texture, including diminishing fine lines and wrinkles, in addition to the essentially immediate improvements in appearance.

CLM What is claimed is:
13. The composition of claim 1 further comprising a **skin** conditioning component.

22. A method of regulating **skin** condition comprising topically applying the composition of claim 1.

23. The method of claim 22 wherein regulating **skin** condition comprises masking imperfections on the **skin** surface.

L7 ANSWER 10 OF 18 USPATFULL
AN 1999:132208 USPATFULL
TI UV protection compositions
IN Robinson, Larry Richard, Loveland, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5972316 19991026 <--
AI US 1999-263017 19990305 (9)
RLI Continuation-in-part of Ser. No. US 1998-174307, filed on 16 Oct 1998, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dodson, Shelley A.
LREP Kendall, Dara M., Henderson, Loretta J., Hilton, Michael E.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 893
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5972316 19991026 <--
SUMM It is well known that exposure to sunlight can pose a number of hazards to the **skin**. These damaging effects may result not only from sunbathing but also from the sunlight exposure associated with daily outdoor activities.. . . a wavelength of from about 290 nm to about 320 nm. Over the long term, however, malignant changes in the **skin** surface often occur. Numerous epideminologic studies

demonstrate a strong relationship between sunlight exposure and human **skin** cancer. Another long term hazard of ultraviolet radiation is premature aging of the **skin**, which is primarily caused by UVA radiation having a wavelength of from about 320 nm to about 400 nm. This condition is characterized by wrinkling and pigment changes of the **skin**, along with other physical changes such as cracking, telangiectasis, solar dermatoses, ecchymoses, and loss of elasticity. The adverse effects associated. . .

SUMM . . . care products" refer to health and cosmetic beauty aid products generally recognized as being formulated for beautifying and grooming the **skin** and hair. For example, personal care products include sunscreen products (e.g., lotions, **skin** creams, etc.), cosmetics, toiletries, and over-the-counter pharmaceutical products intended for topical usage.

SUMM . . . are efficient at absorbing UV radiation in the 290 nm to 320 nm UVB region such that sunburn of the **skin** is prevented. They are less efficient when it comes to absorbing light which falls in the 320 nm to 400 nm UVA region, which leaves the **skin** vulnerable to premature **skin** aging. This deficiency is due in part to the limited number of UVA absorbing sunscreen actives which are both commercially. . .

SUMM . . . there is a need for photostabilized compositions suitable for providing protection against the harmful effects of UV radiation to human **skin**. In particular, in the personal care industry, a need remains for sunscreen products having excellent photostability, efficiency, and which provide. . .

SUMM . . . and most preferably from about 2:1 to about 1:1. The present invention also relates to methods for providing protection to **skin** from the harmful effects of UV radiation by topical application of such compositions. Furthermore, the present invention relates to methods. . .

SUMM . . . compositions of the present invention are useful for providing protection against the harmful effects of ultraviolet radiation, especially to human **skin**. The essential components of these compositions are described below. Also included is a nonexclusive description of various optional and preferred. . .

SUMM . . . against erythema. The SPF is defined as the ratio of the ultraviolet energy required to produce minimal erythema on protected **skin** to that required to produce the same minimal erythema on unprotected **skin** in the same individual. See Federal Register, 43, No. 166, pp. 38206-38269, Aug. 25, 1978).

SUMM . . . use application. For example, carriers of the present invention include, but are not limited to, those suitable for application to **skin**, hair, nails, animal **skin**, fur, automobiles, fabrics, marine vehicles, as well as those suitable for incorporation into plastics, metals, etc. Preferably, the carriers of the present invention are suitable for application to **skin** (e.g., sunscreens, creams, milks, lotions, masks, serums, etc.); hair and fur (e.g., shampoos, hair setting or treatment gels or lotions,. . . lacquers or lotions, etc,); and nails (e.g., polishes, treatments, etc.). In preferred embodiments, the carrier is suitable for application to **skin** which means that the carrier and its components are suitable for use in contact with **skin**, hair, fur, and nails without undue toxicity, incompatibility, instability, allergic response, and the like within the scope of sound medical. . . and can include one or more compatible liquid or solid filler diluents or vehicles which are suitable for application to **skin**, hair, fur, and nails. The exact amount of carrier will depend upon the level of the UVA-absorbing dibenzoylmethane sunscreen active,. . .

SUMM . . . etc.), hair care and styling products (e.g., shampoos, conditioners, gels, mousses, sprays, etc.), topical animal care items (e.g., shampoos, conditioners, **skin** treatments, etc.). Any

additional components required to formulate such products vary with product type and can be routinely chosen by. . .

SUMM If compositions of the present invention are formulated as an aerosol and applied to the **skin** as a spray-on product, a propellant is added to the composition. Examples of suitable propellants include chlorofluorinated lower molecular weight. . .

SUMM In a preferred embodiment, where the composition is to be in contact with human **skin**, the optional components should be suitable for application to **skin**, that is, when incorporated into the composition they are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability, allergic response, and the like within the scope of sound medical judgment. The CTFA Cosmetic Ingredient Handbook, Second Edition (1992) describes a wide variety of nonlimiting cosmetic and pharmaceutical ingredients commonly used in the **skin** care industry, which are suitable for use in the compositions of the present invention. Examples of these ingredient classes include: abrasives, absorbents, aesthetic components such as fragrances, pigments, colorings/colorants, essential oils, **skin** sensates, astringents, etc. (e.g., clove oil, menthol, camphor, eucalyptus oil, eugenol, menthyl lactate, witch hazel distillate), anti-acne agents, anti-caking agents,. . . and substantivity of the composition (e.g., copolymer of eicosene and vinyl pyrrolidone), opacifying agents, pH adjusters, propellants, reducing agents, sequestrants, **skin** bleaching and lightening agents (e.g., hydroquinone, kojic acid, ascorbic acid, magnesium ascorbyl phosphate, ascorbyl glucosamine), **skin**-conditioning agents (e.g., humectants, including miscellaneous and occlusive), **skin** soothing and/or healing agents (e.g., panthenol and derivatives (e.g., ethyl panthenol), aloe vera, pantothenic acid and its derivatives, allantoin, bisabolol, and dipotassium glycyrrhizinate), **skin** treating agents, thickeners, and vitamins and derivatives thereof.

SUMM . . . such optional components. Preferred compositions optionally contain one or more materials selected from UVB sunscreen actives, anti-acne actives, vitamin compounds, **skin** treating agents, humectants, moisturizers, **skin** conditioners, thickening agents, structuring agents, and emulsifiers.

SUMM . . . These vitamin compounds may be in either natural or synthetic form. Suitable vitamin compounds include, but are not limited to, **Vitamin A** (e.g., beta carotene, retinoic acid, retinol, retinoids, retinyl **palmitate**, retinyl proprionate, etc.), Vitamin B (e.g., niacin, niacinamide, riboflavin, pantothenic acid, etc.), **Vitamin C** (e.g., ascorbic acid, etc.), Vitamin D (e.g., ergosterol, ergocalciferol, cholecalciferol, etc.), **Vitamin E** (e.g., tocopherol acetate, etc.), and Vitamin K (e.g., phytonadione, menadione, phthiocol, etc.) compounds.

SUMM In particular, the compositions of the present invention may comprise a safe and effective amount of a **vitamin B.sub .3** compound. **Vitamin B.sub. 3** compounds are particularly useful for regulating **skin** condition as described in co-pending U.S. application Ser. No. 08/834,010, filed Apr. 11, 1997 (corresponding to international publication WO 97/39733. . . and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the **vitamin B.sub.3** compound.

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR12## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B. sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM Examples of suitable **vitamin B.sub.** **3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM d) **Skin** Treating Agent

SUMM The compositions of the present invention may contain one or more **skin** treating agents. Suitable **skin** treating agents include those effective for preventing, retarding, arresting, and/or reversing **skin** wrinkles. Examples of suitable **skin** treating agents include, but are not limited to, alpha-hydroxy acids such as lactic acid and glycolic acid and beta-hydroxy acids. . .

SUMM g) Humectants, Moisturizers, and **Skin** Conditioners

SUMM Preferred compositions optionally comprise one or more humectants, moisturizers, or **skin** conditioners. A variety of these materials can be employed and each can be present at a level of from about. . .

SUMM . . . products. More preferably, the compositions of the present invention are suitable for use as sunscreens to provide protection to human **skin** from the harmful effects of UV radiation which include, but are not limited to, sunburn and premature aging of the **skin**. The present invention therefore also further relates to methods of protecting human **skin** from the harmful effects of UV radiation. Such methods generally involve attenuating or reducing the amount of UV radiation which reaches the **skin**'s surface. To protect the **skin** from UV radiation, a safe and effective (photoprotective) amount of the composition is topically applied to the **skin**. "Topical application" refers to application of the present compositions by spreading, spraying, etc. onto the surface of the **skin**. The exact amount applied may vary depending on the level of UV protection desired. From about 0.5 mg of composition per cm.sup.2 of **skin** to about 25 mg of composition per cm.sup.2 of **skin** are typically applied.

DETD . . . DEA Oleth-3 Phosphate 0.75 0.75 0.75 0.75
Stearic Acid 1.00 1.00 1.00 1.00
Cetyl Alcohol 1.00 1.00 1.00 1.00
Cetyl **Palmitate** 0.50 0.50 0.50 0.50
Triethanolamine 0.70 0.70 1.5 1.5

.sup.1 Available as Pemulen TR1 from B. F. Goodrich

DETD . . . combining octyl methoxycinnamate, octyl salicylate, isopropyl myristate, propyl paraben, 4-phenoxyaniline, 4-chloro-2-methoxy-5-methylaniline, 4-t-butyl-4'-methoxyldibenzoylmethane, DEA oleth-3-phosphate, stearic acid, cetyl alcohol, and cetyl **palmitate** in a separate vessel with mixing and heating to 75.degree. C. Next, mix the oil phase into the water phase. . .

CLM What is claimed is:

. . . effects of ultraviolet radiation, said method comprising applying a safe and effective amount of the composition of claim 1 to **skin** .

L7 ANSWER 11 OF 18 USPATFULL

AN 1999:128146 USPATFULL

TI **Skin** care compositions

IN Deckner, George Endel, Cincinnati, OH, United States
SaNogueira, Jr., James Pedrosa, Wyoming, OH, United States
Zukowski, Joseph Michael, Cincinnati, OH, United States

PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)

PI US 5968528 19991019 <--

AI US 1997-862774 19970523 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Clardy, S. Mark; Assistant Examiner: Williamson, Michael A.
LREP Little, Darryl C., Matthews, Armina E., Allen, George W.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2109
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI **Skin** care compositions
PI US 5968528 19991019 <--
AB Disclosed are **skin** care compositions containing a **vitamin B.sub.3** compound which generally improve the quality of the **skin**, particularly human facial **skin**. More particularly, the present invention relates to niacinamide containing **skin** care compositions with improved **skin** compatibility.
SUMM Invention relates to **skin** care compositions containing a **vitamin B.sub.3** compound which generally improve the quality of the **skin**, particularly human facial **skin**. More particularly, the present invention relates to niacinamide containing **skin** care compositions with improved **skin** compatibility.
SUMM Many personal care products currently available to consumers are directed primarily to improving the health and/or physical appearance of the **skin**. Among these **skin** care products, many are directed to delaying, minimizing or even eliminating **skin** wrinkling and other histological changes typically associated with the aging of **skin** or environmental damage to human **skin**.
SUMM **Skin** is subject to insults by many extrinsic and intrinsic factors. Extrinsic factors include ultraviolet radiation (e.g., from sun exposure), environmental. . . low humidity, harsh surfactants, abrasives, and the like. Intrinsic factors include chronological aging and other biochemical changes from within the **skin**. Whether extrinsic or intrinsic, these factors result in visible signs of **skin** aging and environmental damage, such as wrinkling and other forms of roughness (including increased pore size, flaking and **skin** lines), and other histological changes associated with **skin** aging or damage. To many people, **skin** wrinkles are a reminder of the disappearance of youth. As a result, the elimination of wrinkles has become a booming. . .
SUMM Extrinsic or intrinsic factors may result in the thinning and general degradation of the **skin**. For example, as the **skin** naturally ages, there is a reduction in the cells and blood vessels that supply the **skin**. There is also a flattening of the dermal-epidermal junction which results in weaker mechanical resistance of this junction. See, for example, Oikarinen, "The Aging of **Skin**: Chronoaging Versus Photoaging," Photodermatol. Photoimmunol. Photomed., vol. 7, pp. 3-4, 1990, which is incorporated by reference herein in its entirety.
SUMM **Vitamin B.sub.3** compounds, particularly niacinamide, have recently been found to provide measurable **skin** regulating benefits. For example, topical niacinamide helps to regulate the signs of **skin** aging, i.e., reduce or efface the visibility of the fine lines, wrinkles, and other forms of uneven or rough surface texture associated with aged or photodamaged **skin**. These compounds have also been found useful in reducing the overall oiliness of **skin**.
SUMM In formulating products containing **vitamin B.sub.3** compounds, much attention is directed toward providing compositions which deliver and retain optimal concentrations of the **vitamin B.sub.3** compounds in the stratum corneum with minimum absorption into the systemic

circulation. Furthermore, promoting user compliance with respect to chronic treatment regimens is also important. Current **vitamin B.sub.3** formulations, however, can be drying and irritating. Such formulations may cause individuals to refrain from using **vitamin B.sub.3** products as frequently and copiously as is necessary for optimum benefit.

SUMM The present inventors have found that compositions containing natural or synthetic **vitamin B.sub.3** compounds along with a preservative component comprising a formaldehyde donating preservative and a halopropynyl compound, deliver the **skin** regulating benefits of a **vitamin B.sub.3** compound with reduced dryness and/or irritation. These compositions have improved user acceptance and, thus, promote better user compliance with a concomitant overall improvement in **skin** regulating benefit.

SUMM It is, therefore, an object of the present invention is to provide natural or synthetic **vitamin B.sub.3** containing **skin** care compositions having improved **skin** compatibility.

SUMM Another object of the present invention is to provide natural or synthetic **vitamin B.sub.3** compositions containing preservative systems which provide preservation activity at concentrations of no more than 0.2%.

SUMM Still another object of the present invention is to provide natural or synthetic **vitamin B.sub.3** compositions containing preservative systems which do not substantially impact niacinamide stability or bioavailability.

SUMM The present invention relates to **skin** care compositions, comprising:

SUMM a.) from about 0.01% to about 50% of a **vitamin B.sub.3** compound, and

SUMM The present invention further relates to methods of regulating **skin** conditioning.

SUMM . . . application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the **skin**.

SUMM . . . as used herein, means that the compositions or components thereof so described are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability, allergic response, and the like.

SUMM . . . used herein means an amount of a compound or composition sufficient to significantly induce a positive benefit, preferably a positive **skin** appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to. . .

SUMM The term "**skin** compatibility," as used herein means the ability of **skin** to tolerate long term application of topical compositions with minimal adverse **skin** reactions such as stinging, burning, redness, itching and folliculitis.

SUMM The compositions of the present invention are useful for topical application and for regulating **skin** condition, including visible and/or tactile discontinuities in **skin** (especially the **skin** surface; such discontinuities are generally undesirable). Such discontinuities may be induced or caused by internal and/or external factors, and include the signs of **skin** aging described herein. The term "regulating **skin** condition" includes prophylactically regulating and/or therapeutically regulating **skin** condition, including visible and/or tactile discontinuities in **skin**. As used herein, prophylactically regulating **skin** condition includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in **skin**. As used herein, therapeutically regulating **skin** condition includes

ameliorating, e.g., diminishing, minimizing and/or effacing, discontinuities in **skin**. Regulating **skin** condition involves improving **skin** appearance and/or feel.

SUMM The compositions of the present invention are useful for regulating signs of **skin** aging, more especially visible and/or tactile discontinuities in **skin** texture associated with aging. "Regulating the signs of **skin** aging" includes prophylactically regulating and/or therapeutically regulating one or more of such signs (similarly, regulating a given sign of **skin** aging, e.g., , lines, wrinkles or pores, includes prophylactically regulating and/or therapeutically regulating that sign). As used herein, prophylactically regulating such signs includes delaying, minimizing and/or preventing signs of **skin** aging. As used herein, therapeutically regulating such signs includes ameliorating, e.g., diminishing, minimizing and/or effacing signs of **skin** aging.

SUMM "Signs of **skin** aging" include, but are not limited to, all outward visibly and tactilely perceptible manifestations as well as any other macro or micro effects due to **skin** aging. Such signs may be induced or caused by intrinsic factors or extrinsic factors, e.g., chronological aging and/or environmental damage.. . . not limited to, the development of textural discontinuities such as wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, **skin** lines, crevices, bumps, large pores (e.g., associated with adnexal structures such as sweat gland ducts, sebaceous glands, or hair follicles), scaliness, flakiness and/or other forms of **skin** unevenness or roughness, loss of **skin** elasticity (loss and/or inactivation of functional **skin** elastin), sagging (including puffiness in the eye area and jowls), loss of **skin** firmness, loss of **skin** tightness, loss of **skin** recoil from deformation, discoloration (including undereye circles), blotching, sallowness, hyperpigmented **skin** regions such as age spots and freckles, keratoses, abnormal differentiation, hyperkeratinization, elastosis, collagen breakdown, and other histological changes in the stratum corneum, dermis, epidermis, the **skin** vascular system (e.g., telangiectasia or spider vessels), and underlying tissues, especially those proximate to the **skin**.

SUMM . . . to be understood that the present invention is not to be limited to regulation of the above mentioned "signs of **skin** aging" which arise due to mechanisms associated with **skin** aging, but is intended to include regulation of said signs irrespective of the mechanism of origin. As used herein, "regulating **skin** condition" is intended to include regulation of such signs irrespective of the mechanism of origin.

SUMM The present invention is especially useful for therapeutically regulating visible and/or tactile discontinuities in mammalian **skin** texture, including texture discontinuities associated with **skin** aging. As used herein, therapeutically regulating such discontinuities includes ameliorating, e.g., diminishing, minimizing and/or effacing visible and/or tactile discontinuities in the texture of mammalian **skin**, to thereby provide improved **skin** appearance and/or feel, e.g., a smoother, more even appearance and/or feel. Such visible and/or tactile discontinuities in **skin** texture include crevices, bumps, pores, fine lines, wrinkles, scales, flakes and/or other forms of textural unevenness or roughness associated with **skin** aging. For example, the length, depth, and/or other dimension of lines and/or wrinkles are decreased, the apparent diameter of pores decreases, or the apparent height of tissue immediately proximate to pore openings approaches that of the interadnexal **skin**.

SUMM The present invention is also especially useful for prophylactically regulating visible and/or tactile discontinuities in mammalian **skin** texture, including texture discontinuities associated with

skin aging. As used herein, prophylactically regulating such discontinuities includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in the texture of mammalian **skin** , to thereby provide improved **skin** appearance and/or feel, e.g., a smoother, more even appearance and/or feel.

SUMM **Vitamin B.sub.3** Component

SUMM The compositions of the present invention comprise as a safe and effective amount of a natural or synthetic **vitamin B .sub.3** compound. The compositions of the present invention preferably comprise from about 0.01% to about 50%, more preferably from about 0.1%. . . and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the **vitamin B.sub.3** compound.

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR1## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B. sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM . . . As used herein, "non-rubicient" means that the ester does not commonly yield a visible flushing response after application to the **skin** in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds. . .

SUMM Other derivatives of the **vitamin B.sub. 3** compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of. . .

SUMM . . . esters of the carboxylic acids salicylic acid, acetic acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of **vitamin B.sub.3** compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methyl-nicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)nicotinamide, quinolinic acid imide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid,. . .

SUMM Examples of the above **vitamin B.sub. 3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM One or more **vitamin B.sub.3** compounds may be used herein. Preferred **vitamin B. sub.3** compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

SUMM . . . and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating **skin** condition described herein.

SUMM Salts of the **vitamin B.sub.3** compound are also useful herein. Nonlimiting examples of salts of the **vitamin B.sub.3** compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide,. . . e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the **vitamin B.sub.3** compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic. . .

SUMM In a preferred embodiment, the ring nitrogen of the **vitamin B.sub.3** compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the **skin** becomes substantially chemically free ("chemically free" is

hereinafter alternatively referred to as "uncomplexed"). More preferably, the **vitamin B.sub.3** compound is essentially uncomplexed. Therefore, if the composition contains the **vitamin B.sub.3** compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the **skin**. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility. . .

SUMM More preferably the **vitamin B.sub.3** compound is substantially uncomplexed in the composition prior to delivery to the **skin**. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the **vitamin B.sub.3** compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the **vitamin B.sub.3** compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill. . .

SUMM Thus, in a preferred embodiment, the **vitamin B.sub.3** compound contains a limited amount of the salt form and is more preferably substantially free of salts of a **vitamin B.sub.3** compound. Preferably the **vitamin B.sub.3** compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The **vitamin B.sub.3** compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about. . .

SUMM The **vitamin B.sub.3** compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The **vitamin B.sub.3** compound is preferably substantially pure, more preferably essentially pure.

SUMM . . . use in personal care products. Such products preferably are not odiferous or an irritant or toxic when applied to the **skin**. Examples of suitable formaldehyde donors include dimethyloldimethylhydantoin, N,N"-methylene bis [N'-[hydroxymethyl)-2,5-dioxo-4-imidazolidinyl]urea]; N-(hydroxymethyl)-N-(1,3-dihydroxymethyl-2,5-dioxo-4-imidazolidinyl)-N'-(hydroxymethyl)urea; the cis isomer of 1-(3-chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride, sodium hydroxymethylglycinate, dimethyl. . .

SUMM . . . about 99.5% of a dermatologically acceptable carrier within which the compositions of the present invention is incorporated to enable the **vitamin B.sub.3** compound and preservative component, as well as other optional actives, to be delivered to the **skin** at an appropriate concentration.

SUMM . . . Science and Technology, 2nd Edition, Vol. 2, pp. 443-465 (1972), incorporated herein by reference. Aerosols are typically applied to the **skin** as a spray-on product.

SUMM . . . acceptable emollient. Such compositions preferably contain from about 2% to about 50% of the emollient. Emollients tend to lubricate the **skin**, increase the smoothness and suppleness of the **skin**, prevent or relieve dryness of the **skin**, and/or protect the **skin**. Emollients are typically water-immiscible, oily or waxy materials. A wide variety of suitable emollients are known and may be used. . .

SUMM . . . mousses. Toilet bars are most preferred since this is the form of cleansing agent most commonly used to wash the **skin**. Preferred rinse-off cleansing compositions, such as shampoos, include a

delivery system adequate to deposit sufficient levels of actives on the **skin** and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure of such delivery. . .

SUMM As used herein, the term "foundation" refers to a liquid, semi-liquid, semi-solid, or solid **skin** cosmetic which includes, but is not limited to lotions, creams, gels, pastes, cakes, and the like. Typically the foundation is used over a large area of the **skin**, such as over the face, to provide a particular look. Foundations are typically used to provide an adherent base for color cosmetics such as rouge, blusher, powder and the like, and tend to hide **skin** imperfections and impart a smooth, even appearance to the **skin** . Foundations of the present invention include a dermatologically acceptable carrier for the essential particulate material and may include conventional ingredients. . .

SUMM . . . melting point of about 25.degree. C. or less under about one atmosphere of pressure, and are suitable for conditioning the **skin** or hair.

SUMM . . . acids include straight chain, branched chain and aryl carboxylic acids).. Nonlimiting examples include diisopropyl sebacate, diisopropyl adipate, isopropyl myristate, isopropyl **palmitate**, methyl **palmitate**, myristyl propionate, 2-ethylhexyl **palmitate**, isodecyl neopentanoate, di-2-ethylhexyl maleate, cetyl **palmitate**, myristyl myristate, stearyl stearate, isopropyl stearate, methyl stearate, cetyl stearate, behenyl behenrate, dioctyl maleate, dioctyl sebacate, diisopropyl adipate, cetyl octanoate,. . .

SUMM . . . cosmetic biocides, denaturants, cosmetic astringents, drug astringents, external analgesics, film formers, humectants, opacifying agents, fragrances, perfumes, pigments, colorings, essential oils, **skin** sensates, emollients, **skin** soothing agents, **skin** healing agents, pH adjusters, plasticizers, preservatives, preservative enhancers, propellants, reducing agents, **skin** -conditioning agents, **skin** penetration enhancing agents, **skin** protectants, solvents, suspending agents, emulsifiers, thickening agents, solubilizing agents, polymers for aiding the film-forming properties and substantivity of the composition. . . anti-androgens, depilation agents, desquamation agents/exfoliants, organic hydroxy acids, vitamins and derivatives thereof (including water dispersible or soluble vitamins such as **Vitamin C** and ascorbyl phosphates), compounds which stimulate collagen production, and natural extracts. Such other materials are known in the art. Nonexclusive. . .

SUMM In a preferred embodiment, the composition also includes an active useful for chronically regulating **skin** condition. Such materials are those which manifest **skin** appearance benefits following chronic application of the composition containing such materials. Materials having this effect include, but are not limited. . .

SUMM In a preferred embodiment, the compositions of the present invention contain a retinoid. The retinoid enhances the **skin** appearance benefits of the present invention, especially in regulating **skin** condition, including regulating signs of **skin** aging, more especially wrinkles, lines, and pores.

SUMM As used herein, "retinoid" includes all natural and/or synthetic analogs of **Vitamin A** or retinol-like compounds which possess the biological activity of **Vitamin A** in the **skin** as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably retinol, retinol esters (e.g., C.sub.2 -C.sub.22 alkyl esters of retinol, including retinyl **palmitate**, retinyl acetate, retinyl propionate), retinal, and/or retinoic acid (including all-trans retinoic acid and/or 13-cis-retinoic

acid), more preferably retinoids other than. . . adapalene {6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid}, and tazarotene (ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)-ethynyl]nicotinate). One or more retinoids may be used herein. Preferred retinoids are retinol, retinyl **palmitate**, retinyl acetate, retinyl proprionate, retinal and combinations thereof. More preferred are retinol and retinyl **palmitate**.

SUMM . . . contain a safe and effective amount of the retinoid, such that the resultant composition is safe and effective for regulating **skin** condition, preferably for regulating visible and/or tactile discontinuities in **skin**, more preferably for regulating signs of **skin** aging, even more preferably for regulating visible and/or tactile discontinuities in **skin** texture associated with **skin** aging. The compositions preferably contain from or about 0.005% to or about 2%, more preferably 0.01% to or about 2%,. . .

SUMM In a preferred embodiment, the composition contains both a retinoid and a **Vitamin B.sub.3** compound. The retinoid is preferably used in the above amounts, and the **vitamin B.sub.3** compound is preferably used in an amount of from or about 0.1% to or about 10%, more preferably from or. . .

SUMM . . . 0.1% to about 10%, more preferably from about 0.5% to about 5%, of the composition. The anti-inflammatory agent enhances the **skin** appearance benefits of the present invention, e.g., such agents contribute to a more uniform and acceptable **skin** tone or color. The exact amount of anti-inflammatory agent to be used in the compositions will depend on the particular. . .

SUMM An agent may also be added to any of the compositions useful in the subject invention to improve the **skin** substantivity of those compositions, particularly to enhance their resistance to being washed off by water, or rubbed off. A preferred. . .

SUMM . . . which can cause increased scaling or texture changes in the stratum corneum and against other environmental agents which can cause **skin** damage.

SUMM Anti-oxidants/radical scavengers such as ascorbic acid (**vitamin C**) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate), tocopherol (**vitamin E**), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under. . . acid and its salts, lycine pidolate, arginine pilolate, nordihydroguaiaretic acid, bioflavonoids, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape **skin**/seed extracts, melanin, and rosemary extracts may be used. Preferred anti-oxidants/radical scavengers are selected from tocopherol sorbate and other esters of. . .

SUMM . . . of a chelating agent is especially useful for providing protection against UV radiation which can contribute to excessive scaling or **skin** texture changes and against other environmental agents which can cause **skin** damage.

SUMM . . . about 5%, also preferably from about 0.5% to about 2%. Salicylic acid is preferred. The organic hydroxy acids enhance the **skin** appearance benefits of the present invention. For example, the organic hydroxy acids tend to improve the texture of the **skin**.

SUMM . . . about 0.2% to about 5%, also preferably from about 0.5% to about 4% of the composition. Desquamation agents enhance the **skin** appearance benefits of the present invention. For example, the desquamation agents tend to improve the texture of the **skin** (e.g., smoothness). A variety of desquamation agents are known in the art and are suitable for use herein, including but. . .

SUMM H. **Skin** Lightening Agents

SUMM The compositions of the present invention may comprise a **skin** lightening agent. When used, the compositions preferably comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%, of a **skin** lightening agent. Suitable **skin** lightening agents include those known in the art, including kojic acid, arbutin, ascorbic acid and derivatives thereof, e.g., magnesium ascorbyl phosphate. **Skin** lightening agents suitable for use herein also include those described in copending patent application Ser. No. 08/479,935, filed on Jun.. . .

SUMM I. **Skin** Conditioners

SUMM Preferred compositions of the invention comprise an optional **skin** conditioning component. The **skin** conditioning component is preferably selected from the group consisting of emollients, humectants, moisturizers and mixtures thereof. The **skin** conditioning component is preferably present at a level of at least about 0.1%, more preferably from about 1% to about. . .

SUMM . . . but are not limited to, methyl, isopropyl, and butyl esters of fatty acids such as hexyl laurate, isohexyl laurate, isohexyl **palmitate**, isopropyl **palmitate**, methyl **palmitate**, decyloleate, isodecyl oleate, hexadecyl stearate decyl stearate, isopropyl isostearate, methyl isostearate, diisopropyl adipate, diisohexyl adipate, dihexyldecyl adipate, diisopropyl sebacate, lauryl. . .

SUMM Methods for Regulating **Skin** Condition

SUMM The compositions of the present invention are useful for regulating mammalian **skin** condition (especially human **skin**, more especially human facial **skin**), including visible and/or tactile discontinuities in **skin**, signs of **skin** aging, and visible and/or tactile discontinuities in **skin** associated with **skin** aging (including fine lines, wrinkles, large pores, surface roughness and other texture discontinuities associated with aged **skin**). Such regulation includes prophylactic and therapeutic regulation.

SUMM Regulating **skin** condition involves topically applying to the **skin** a safe and effective amount of a composition of the present invention. The amount of the composition which is applied, the frequency of application and the period of use will vary widely depending upon the level of **vitamin B.sub.3** compound and/or other components of a given composition and the level of regulation desired, e.g., in light of the level of **skin** aging present in the subject and the rate of further **skin** aging.

SUMM In a preferred embodiment, the composition is chronically applied to the **skin**. By "chronic topical application" is meant continued topical application of the composition over an extended period during the subject's lifetime,. . .

SUMM A wide range of quantities of the compositions of the present invention can be employed to provide a **skin** appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm.sup.2 **skin**, from about 0.1 mg/cm.sup.2 to about 10 mg/cm.sup.2. A particularly useful application amount is about 2 mg/cm.sup.2.

SUMM Regulating **skin** condition is preferably practiced by applying a composition in the form of a **skin** lotion, cream, cosmetic, or the like which is intended to be left on the **skin** for some esthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition). After applying the composition to the **skin**, it is preferably left on the **skin** for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at. . .

DETD

Ingredient	Weight Percent

Phase A
DI water 14.699
glycerin 10.000
Phase B Carbopol 954 0.400
disodium EDTA 0.100
Phase C isopropyl **palmitate** 0.400
cetyl alcohol 2.300
cyclomethicone/dimethicone copolyol 1.900
stearyl alcohol 1.500
dimethicone (200 cts) 0.600
PEG 100 Stearate 0.300
stearic acid 0.300
cetyl **palmitate** 2.500
Phase D DI water 3.000
sodium hydroxide 0.200
Phase E DI water 8.000
Niacinamide 2.000
Phase F Sodium hydroxy glycinate 0.100
Isopropynyl butylcarbamide 0.100
DI water 0.300
butylene glycol 0.300
Phase G isopropyl **palmitate** 1.000
retinol 0.050
BHT 0.001
Polysorbate 20 0.050

DETD The resulting composition is useful for application to the **skin** for delivering the retinol and to treat and improve the appearance of the **skin**.

DETD . . . niacinamide 2.000
Phase E N,N"-methylene bis[N'-[(Hydroxymethyl)-2,5,- 0.100
dioxy-4-imidazolodinyl]urea]
DI water 0.300
Isopropynyl butylcarbamide 0.005
butylene glycol 0.300
Phase F Isopropyl **palmitate** 1.000
retinol 0.050
BHT 0.001
Polysorbate 20 0.050

DETD The resulting composition is useful for application to the **skin** for delivering the actives and to treat and improve the appearance of the **skin**.

CLM What is claimed is:

1. **Skin** care compositions comprising: a.) from about 2% to about 5% of niacinamide; b.) from about 0.05% to about 0.2% of. . .

6. A method of regulating **skin** condition, which method comprises applying to the **skin** of a mammal a safe and effective amount of the composition according to claim 1.

7. A method of regulating visible and/or tactile discontinuities in the texture of mammalian **skin**, comprising applying to the **skin** of a mammal a safe and effective amount of the composition according to claim 1.

L7 ANSWER 12 OF 18 USPATFULL
AN 1999:128104 USPATFULL
TI UV protection compositions
IN Robinson, Larry Richard, Loveland, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S.

corporation)
PI US 5968485 19991019 <--
AI US 1999-263673 19990305 (9)
RLI Continuation-in-part of Ser. No. US 1998-174274, filed on 16 Oct 1998, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dodson, Shelley A.
LREP Kendall, Dara M., Henderson, Loretta J., Hilton, Michael E.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 903
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5968485 19991019 <--

SUMM It is well known that exposure to sunlight can pose a number of hazards to the **skin**. These damaging effects may result not only from sunbathing but also from the sunlight exposure associated with daily outdoor activities.. . . a wavelength of from about 290 nm to about 320 nm. Over the long term, however, malignant changes in the **skin** surface often occur. Numerous epideminologic studies demonstrate a strong relationship between sunlight exposure and human **skin** cancer. Another long term hazard of ultraviolet radiation is premature aging of the **skin**, which is primarily caused by UVA radiation having a wavelength of from about 320 nm to about 400 nm. This condition is characterized by wrinkling and pigment changes of the **skin**, along with other physical changes such as cracking, telangiectasis, solar dermatoses, ecchymoses, and loss of elasticity. The adverse effects associated. . .

SUMM . . . care products" refer to health and cosmetic beauty aid products generally recognized as being formulated for beautifying and grooming the **skin** and hair. For example, personal care products include sunscreen products (e.g., lotions, **skin** creams, etc.), cosmetics, toiletries, and over-the-counter pharmaceutical products intended for topical usage.

SUMM . . . are efficient at absorbing UV radiation in the 290 nm to 320 nm UVB region such that sunburn of the **skin** is prevented. They are less efficient when it comes to absorbing light which falls in the 320 nm to 400 nm UVA region, which leaves the **skin** vulnerable to premature **skin** aging. This deficiency is due in part to the limited number of UVA absorbing sunscreen actives which are both commercially. . .

SUMM . . . there is a need for photostabilized compositions suitable for providing protection against the harmful effects of UV radiation to human **skin**. In particular, in the personal care industry, a need remains for sunscreen products having excellent photostability, efficiency, and which provide. . .

SUMM . . . and most preferably from about 2:1 to about 1:1. The present invention also relates to methods for providing protection to **skin** from the harmful effects of UV radiation by topical application of such compositions. Furthermore, the present invention relates to methods. . .

SUMM . . . compositions of the present invention are useful for providing protection against the harmful effects of ultraviolet radiation, especially to human **skin**. The essential components of these compositions are described below. Also included is a nonexclusive description of various optional and preferred. . .

SUMM . . . against erythema. The SPF is defined as the ratio of the ultraviolet energy required to produce minimal erythema on protected **skin** to that required to produce the same minimal erythema on unprotected **skin** in the same individual. See Federal Register, 43, No. 166, pp. 38206-38269, Aug. 25, 1978).

SUMM . . . use application. For example, carriers of the present invention include, but are not limited to, those suitable for application to **skin**, hair, nails, animal **skin**, fur, automobiles, fabrics, marine vehicles, as well as those suitable for incorporation into plastics, metals, etc. Preferably, the carriers of the present invention are suitable for application to **skin** (e.g., sunscreens, creams, milks, lotions, masks, serums, etc.); hair and fur (e.g., shampoos, hair setting or treatment gels or lotions,. . . lacquers or lotions, etc,); and nails (e.g., polishes, treatments, etc.). In preferred embodiments, the carrier is suitable for application to **skin** which means that the carrier and its components are suitable for use in contact with **skin**, hair, fur, and nails without undue toxicity, incompatibility, instability, allergic response, and the like within the scope of sound medical. . . and can include one or more compatible liquid or solid filler diluents or vehicles which are suitable for application to **skin**, hair, fur, and nails. The exact amount of carrier will depend upon the level of the UVA-absorbing dibenzoylmethane sunscreen active,. . .

SUMM . . . etc.), hair care and styling products (e.g., shampoos, conditioners, gels, mousses, sprays, etc.), topical animal care items (e.g., shampoos, conditioners, **skin** treatments, etc.). Any additional components required to formulate such products vary with product type and can be routinely chosen by. . .

SUMM If compositions of the present invention are formulated as an aerosol and applied to the **skin** as a spray-on product, a propellant is added to the composition. Examples of suitable propellants include chlorofluorinated lower molecular weight. . .

SUMM In a preferred embodiment, where the composition is to be in contact with human **skin**, the optional components should be suitable for application to **skin**, that is, when incorporated into the composition they are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability, allergic response, and the like within the scope of sound medical judgment. The CTFA Cosmetic Ingredient Handbook, Second Edition (1992) describes a wide variety of nonlimiting, cosmetic and pharmaceutical ingredients commonly used in the **skin** care industry, which are suitable for use in the compositions of the present invention. Examples of these ingredient classes include: abrasives, absorbents, aesthetic components such as fragrances, pigments, colorings colorants, essential oils, **skin** sensates, astringents, etc. (e.g., clove oil, menthol, camphor, eucalyptus oil, eugenol, menthyl lactate, witch hazel distillate), anti-acne agents, anti-caking agents,. . . and substantivity of the composition (e.g., copolymer of eicosene and vinyl pyrrolidone), opacifying agents, pH adjusters, propellants, reducing agents, sequestrants, **skin** bleaching and lightening agents (e.g., hydroquinone, kojic acid, ascorbic acid, magnesium ascorbyl phosphate, ascorbyl glucosamine), **skin**-conditioning agents (e.g., humectants, including miscellaneous and occlusive), **skin** soothing and/or healing agent (e.g., panthenol and derivatives (e.g., ethyl panthenol), aloe vera, pantothenic acid and its derivatives, allantoin, bisabolol, and dipotassium glycyrrhizinate), **skin** treating agents, thickeners, and vitamins and derivatives thereof.

SUMM . . . such optional components. Preferred compositions optionally contain one or more materials selected from UVB sunscreen actives, anti-acne actives, vitamin compounds, **skin** treating agents, humectants, moisturizers, **skin** conditioners, thickening agents, structuring agents, and emulsifiers.

SUMM . . . These vitamin compounds may be in either natural or synthetic form. Suitable vitamin compounds include, but are not limited to, **Vitamin A** (e.g., beta carotene, retinoic acid, retinol, retinoids, retinyl **palmitate**, retinyl proprionate, etc.), Vitamin B (e.g., niacin, niacinamide, riboflavin, pantothenic

acid, etc.), **Vitamin C** (e.g., ascorbic acid, etc.), Vitamin D (e.g., ergosterol, ergocalciferol, cholecalciferol, etc.), **Vitamin E** (e.g., tocopherol acetate, etc), and Vitamin K (e.g., phytonadione, menadione, phthiocol, etc.) compounds.

SUMM In particular, the compositions of the present invention may comprise a safe and effective amount of a **vitamin B.sub .3** compound. **Vitamin B.sub. 3** compounds are particularly useful for regulating **skin** condition as described in co-pending U.S. application Ser. No. 08/834,010, filed Apr. 11, 1997 (corresponding to international publication WO 97/39733. . . and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the **vitamin B.sub.3** compound.

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR7## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B. sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM Examples of suitable **vitamin B.sub. 3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM d) **Skin** Treating Agent

SUMM The compositions of the present invention may contain one or more **skin** treating agents. Suitable **skin** treating agents include those effective for preventing, retarding, arresting, and/or reversing **skin** wrinkles. Examples of suitable **skin** treating agents include, but are not limited to, alpha-hydroxy acids such as lactic acid and glycolic acid and beta-hydroxy acids. . .

SUMM g) Humectants, Moisturizers, and **Skin** Conditioners

SUMM Preferred compositions optionally comprise one or more humectants, moisturizers, or **skin** conditioners. A variety of these materials can be employed and each can be present at a level of from about. . .

SUMM . . . products. More preferably, the compositions of the present invention are suitable for use as sunscreens to provide protection to human **skin** from the harmful effects of UV radiation which include, but are not limited to, sunburn and premature aging of the **skin**. The present invention therefore also further relates to methods of protecting human **skin** from the harmful effects of UV radiation. Such methods generally involve attenuating or reducing the amount of UV radiation which reaches the **skin**'s surface. To protect the **skin** from UV radiation, a safe and effective (photoprotective) amount of the composition is topically applied to the **skin**. "Topical application" refers to application of the present compositions by spreading, spraying, etc. onto the surface of the **skin**. The exact amount applied may vary depending on the level of UV protection desired. From about 0.5 mg of composition per cm.sup.2 of **skin** to about 25 mg of composition per cm.sup.2 of **skin** are typically applied.

DETD . . . DEA Oleth-3 Phosphate 0.75 0.75 0.75 0.75
Stearic Acid 1.00 1.00 1.00 1.00
Cetyl Alcohol 1.00 1.00 1.00 1.00
Cetyl **Palmitate** 0.50 0.50 0.50 0.50
Triethanolamine 0.70 0.70 1.5 1.5

.sup.1 Available as Pemulen TR1 from B. F. Goodrich

DETD . . . salicylate, isopropyl myristate, propyl paraben, triphenylamine, 1-methyl-2-phenylindole, 4-t-butyl-4'-methoxyldibenzoylmethane, the DEA oleth-3-phosphate, the stearic acid,

the cetyl alcohol, and the cetyl **palmitate** in a separate vessel with mixing and heating to 75.degree. C. Next, mix the oil phase into the water phase. . .

CLM What is claimed:
18. A method for protecting **skin** from the harmful effects of ultraviolet radiation, said method comprising applying a safe and effective amount of the composition of claim 1 to **skin**.

L7 ANSWER 13 OF 18 USPATFULL
AN 1999:121419 USPATFULL
TI Pharmaceutical compositions and methods for treating acne
IN Murad, Howard, 4316 Marina City Dr., Marina del Rey, CA, United States 90292
PI US 5962517 19991005 <--
AI US 1998-16800 19980130 (9)
PRAI US 1997-36825P 19970131 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: MacMillan, Keith D.; Assistant Examiner: Kim, Vickie
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 960
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5962517 19991005 <--
AB . . . blemishes associated with acne. The invention also relates to pharmaceutical compositions having, in addition to the acne reduction component, a **skin** cell conditioning component in an amount sufficient to properly regulate the keratin and sebum production of the **skin** cells, thereby inhibiting the appearance of acne. In a preferred form, the **skin** cell conditioning component is a chromium component. In another preferred form, the composition further includes at least one of a **vitamin C** source, burdock root, yellow dock root, horsetail extract, a catechin-based composition, a vitamin B.sub.1 source, a vitamin B.sub.2 source, a **vitamin B.sub.3** source, a vitamin B.sub.5 source, and a **vitamin E** source. In a more preferred form, the invention also includes at least one amino acid component, a magnesium component, a. . . amount therapeutically effective in reducing the incidence of acne and methods for additionally inhibiting the appearance of acne by conditioning **skin** cells.
SUMM This invention relates to pharmaceutical compositions for treating acne and conditioning the **skin** cells in patients. The invention further relates to methods of treating acne and conditioning **skin** cells by administering the pharmaceutical compositions to the patient.
SUMM The mammalian **skin**, in particular, human **skin**, is a multifunctional organ. Not only does the **skin** provide an external covering to protect the body, but it also performs several specialized functions, such as breathing, perspiring, sensory. . . production. [D. Mowery, The Scientific Validation of Herbal Medicine, 248 (1986)]. Oil production, essential to the protective features of the **skin**, works when an oily substance known as sebum is released from the sebaceous glands, which are large glands located at the base of a hair follicle. This permits the **skin** to moisturize and waterproof itself, thereby protecting itself from the environment. [J. Whitaker, Dr. Whitaker's Guide to Natural Healing, 141,. . .
SUMM . . . insoluble protein that is the primary constituent of the hair and the epidermis. Together, the sebum and keratin block a **skin** pore, resulting in a comedone, also known as a blackhead. Bacteria

proliferates in clogged pores, and the body typically responds. . .

SUMM . . . the gland, mixes with dead cells, and eventually ruptures the follicle wall, which typically forms a deep cyst under the **skin** . Scarring often results from these deep cysts. [Roche Laboratories Inc., Important Information Concerning Your Treatment with Accutane, 6th ed., (1996)].. . .

SUMM . . . benzoyl peroxide, erythromycin, clindamycin, or tetracycline are commonly used to control the bacteria. These methods often lead to overly dry **skin**, and relapse is common after treatment has ended. [Id.].

SUMM Vitamins and herbs often provide more promising results with regard to acne. **Vitamin A** has proven to be highly effective in treating acne. Since the early seventies, topical retinoic acid or tretinoin, both derivatives of **vitamin A**, have been used to treat acne topically. [Id.]. These topical agents work by normalizing the **skin**'s production of keratin and the sebaceous glands production of sebum, thereby preventing obstruction of the follicle. Although highly effective, the. . .

SUMM A systemic **vitamin A** derivative for the treatment of nodular acne, known as isotretinoin, is commercially available under the name ACCUTANE.RTM., from Roche Laboratories. . .

SUMM . . . because of its ability to aid in wound healing, immune response, inflammation control, tissue regeneration, and more effective utilization of **vitamin A**. Certain studies have shown that zinc produces results similar to tetracycline in the treatment of superficial acne, but far superior. . . acne. [J. Whitaker, Dr. Whitaker's Guide to Natural Healing, 142 (1995)]. Also, certain nutrients, such as vitamin B.sub.6, selenium, and **vitamin E**, are thought necessary to healthy **skin** and, therefore, control acne. [Id.].

SUMM . . . 158 (1988)]. Additionally, herbs possessing antibiotic properties, such as burdock root and horsetail, may individually aid in the treatment of **skin** blemishes, such as acne. [D. Mowery, The Scientific Validation of Herbal Medicine, 32-33 (1986)].

SUMM . . . company, has been used in conjunction with a cleanser and topical cream to treat acne. The nutritional supplement contains zinc, **vitamin A**, **vitamin C**, and other natural elements that are believed to nourish the **skin**. Also, it is suggested that high doses of **vitamin A** are not needed in AKNE-ZYME.TM. as long as other nutritional factors such as zinc, vitamin B.sub.6, selenium, and **vitamin E** are incorporated into the acne treatment. [J. Whitaker, Dr. Whitaker's Guide to Natural Healing, 141-142 (1995)].

SUMM . . . that the herbal extract be used in conjunction with supplements of one or more of the following nutrients and minerals: **vitamin A**, vitamin B.sub.1, vitamin B.sub.2, vitamin B.sub.6, vitamin B complex, **vitamin C**, vitamin D, **vitamin E**, niacinamide, pantothenic acid, para-aminobenzoic acid, biotin, choline, inositol, folic acid, zinc, calcium, magnesium, and potassium. The reference further notes the. . .

SUMM . . . the above references disclose methods of treating acne, the treatments often involve adverse side effects, such as overdrying of the **skin**. Furthermore, the above treatments simply address the acne and fail to condition the **skin** cells to assist in the treatment and to reduce further incidences of acne. Thus, it is desired to find pharmaceutical compositions and methods for treating acne by administering the pharmaceutical compositions and conditioning the **skin** to inhibit further acne outbreaks without the adverse side effects present in many conventional acne treatments. The present invention, through a blend of herbal extracts and nutritional supplements, advantageously treats acne without adverse side effects, and conditions **skin** cells to reduce the likelihood of further

acne.

SUMM . . . comprising an acne reduction component in an amount sufficient to reduce the redness and blemishes associated with acne and a **skin** cell conditioning component in an amount sufficient to properly regulate the keratin and sebum production of the **skin** cells to inhibit the appearance of acne.

SUMM The **skin** cell conditioning component comprises a transition metal complex with an organic compound. In a preferred embodiment, the transition metal is. . .

SUMM The acne reduction component is a **vitamin A** source, a carotenoid component, a vitamin B.sub.6 source, and a zinc component. In a preferred embodiment, the **vitamin A** source is **vitamin A** complexed with an acetate or **palmitate**, the carotenoid component is beta-carotene, the vitamin B.sub.6 source is a pyridoxine, and the zinc component is zinc complexed with ascorbic acid or ascorbate. In a more preferred embodiment, the **vitamin A** source is **vitamin A palmitate** present in about 0.005 to 5 weight percent, beta-carotene is present in about 0.1 to 10 weight percent, the pyridoxine. . .

SUMM Another embodiment of the pharmaceutical composition also has at least one of a **vitamin C** source, burdock root, yellow dock root, horsetail extract, a catechin-based composition, a vitamin B.sub.1 source, a vitamin B.sub.2 source, a **vitamin B.sub.3** source, a vitamin B.sub.5 source, and a **vitamin E** source, all in an amount sufficient to facilitate maintenance of **skin** cells. In a preferred embodiment, the **vitamin C** source is ascorbic acid or ascorbate, the catechin-based composition is a proanthanol or proanthocyanidin, the vitamin B.sub.1 source is thiamin, the vitamin B.sub.2 source is riboflavin, the **vitamin B.sub.3** source is niacinamide, the vitamin B.sub.5 source is pantothenic acid, and the **vitamin E** source is a sulfate or succinate **vitamin E** complex. In a more preferred embodiment, the **vitamin C** source is calcium ascorbate present in about 1 to 30 weight percent, the burdock root is present in about 1. . . in about 0.05 to 5 weight percent, the thiamin is present in about 0.05 to 5 weight percent and the **vitamin E** source is **vitamin E** succinate present in about 1 to 30 weight percent.

SUMM . . . one amino acid component, a magnesium component, a selenium component, and biotin in an amount sufficient to facilitate repair of **skin** damaged by acne. In a preferred embodiment, the amino acid component is L-lysine and L-proline, the magnesium component is magnesium. . .

SUMM . . . effective to reduce the redness and blemishes associated with acne. In addition, the invention relates to a method for conditioning **skin** cells in a treatment for acne, by administering these pharmaceutical compositions in an amount therapeutically effective to condition the **skin** to assist in reducing the redness and blemishes associated with acne.

SUMM . . . conjunction with concurrent or subsequent treatment by at least an additional pharmaceutical composition used to treat acne or condition the **skin**. In a preferred embodiment, the additional pharmaceutical composition is a topical application having at least one of: alcohol, benzoyl peroxide, erythromycin, clindamycin, tretinoin, **vitamin E**, and **vitamin A** or its derivatives; or an oral application having at least one of: erythromycin, tetracycline, isotretinoin, **vitamin C**, vitamin D, chaparral, dandelion root, licorice root, echinacea, kelp, cayenne, sassafras, elder flowers, pantothenic acid, para-aminobenzoic acid, biotin, choline, inositol, folic acid, calcium, magnesium,

potassium and **Vitamin A** derivatives.

SUMM A pharmaceutical composition for treating acne and conditioning the **skin** cells has now been discovered. The pharmaceutical composition includes an acne reducing component in an amount sufficient to reduce the redness and blemishes associated with acne. Additionally, the present invention preferably includes a **skin** cell conditioning component in an amount sufficient to properly regulate the keratin and sebum production of the **skin** cells, thereby inhibiting or preventing the appearance of acne. The present pharmaceutical composition advantageously treats acne and conditions **skin** cells with reduced adverse side effects compared to conventional acne compositions and treatment methods. Also, the present invention relates to. . .

SUMM . . . present invention reduces acne in a patient by providing an acne reduction component that includes at least one of a **vitamin A** source, a carotenoid component, a vitamin B.sub.6 source, and a zinc component, in an amount sufficient to reduce the redness. . .

SUMM . . . associated with acne. Furthermore, the ability of zinc to aid in wound healing, immune response, tissue regeneration, and utilization of **vitamin A** make it an effective component in the composition and for the treatment of acne according to the invention. The zinc. . .

SUMM **Vitamin A** is necessary for healthy **skin** cell growth and tissue formation. Its function is to inhibit the production of excess **skin** cells that eventually flake off and tend to clog pores. The **vitamin A** source preferably is **vitamin A** complexed to an acetate or **palmitate**, and more preferably is **vitamin A palmitate**. The **vitamin A** source is present in about 0.005 to 5 weight percent, preferably in about 0.07 to 3 weight percent, more preferably in about 0.1 to 2 weight percent of the composition. A unit dose of the **vitamin A** source is typically about 0.1 to 5 mg, preferably about 0.5 to 4 mg, and more preferably is about 1 to 3 mg. **Vitamin A** is toxic at high levels, such that if **vitamin A** is taken in doses of more than 50,000 IU per day over a period of several months it can produce. . .

SUMM . . . such as beta-carotene, canthaxanthin, zeaxanthin, lycopen, lutein, crocetin, and capsanthin. Beta-carotene is a carotenoid that is predominantly found in the **skin**. Beta-carotene protects the integrity of the **skin** cells' structure, fights various **skin** conditions, and enhances the immune system. Carotenoids, preferably beta-carotene, are present in the pharmaceutical composition at about 0.1 to 10. . .

SUMM The present invention, in addition to the acne reducing component, preferably contains a **skin** cell conditioning component in an amount sufficient to properly regulate the sebum in the sebaceous glands and keratin production of the **skin** cells. This preferred embodiment of the pharmaceutical composition may be administered by any means, although oral administration is preferred.

SUMM The **skin** cell conditioning component activates enzymes that are involved in fat and glucose metabolism, which assists the **skin** cells in regulating the production of keratin and sebum. These enzymes increase the glucose intake of cells, thereby increasing the. . . Thus, the present invention attempts to prevent further acne breakouts by encouraging optimal performance of the sebaceous glands. Preferably, the **skin** cell conditioning component is a transition metal complex with an organic compound. Any transition metal can be used but those. . .

SUMM The **skin** cell conditioning component is present in about 0.001 to 5 weight percent, preferably about 0.002 to 3 weight percent, and more preferably about 0.005 to 1 weight percent of the pharmaceutical

composition. A unit dose of the **skin** cell conditioning, such as a chromium component, is about 0.01 mg to 24 mg, preferably about 0.03 mg to 18. . .

SUMM The present invention more preferably contains at least one of the following: a **vitamin C** source, burdock root, yellow dock root, horsetail extract, a catechin-based component, a **vitamin B.sub.3** source, a vitamin B.sub.5 source, a vitamin B.sub.2 source, and a **vitamin E** source to aid in the maintenance of the **skin** cells.

SUMM The pharmaceutical composition includes a **vitamin C** source that includes an ascorbic acid, or pharmaceutically acceptable salt or ester thereof, and preferably includes ascorbyl **palmitate**, dipalmitate L-ascorbate, sodium L-ascorbate-2-sulfate, or an ascorbic salt, such as sodium, potassium, and calcium, or mixtures thereof. More preferably, the. . . is calcium ascorbate. When oral formulations of the pharmaceutical composition are used, it is preferred that a non-acidic form of **vitamin C** be used to reduce the stomach irritation that may occur when using an acidic form. The **vitamin C** source is present in the pharmaceutical composition in about 1 to 30 weight percent, preferably about 5 to 25 weight percent, and more preferably about 10 to 20 weight percent. A unit dose of this **vitamin C** source is typically about 50 mg to 800 mg, preferably about 60 mg to 600 mg, and more preferably about. . .

SUMM Yellow Dock, whose scientific name is Rumex crispus, is often used to treat **skin** disease, especially those involving some form of inflammation. The active constituents of yellow dock are rumicin and chrysarobin. Yellow Dock. . .

SUMM . . . that contains silica, starch, volatile oils, resin, and equisetic acid as active components. This herbal extract aids in detoxifying the **skin**, and also possesses antibiotic properties. Horsetail extract is present in about 1 to 20 weight percent, preferably about 2 to. . .

SUMM . . . within the pharmaceutical composition provides powerful antioxidants to scavenge free radicals. These antioxidants are approximately 20 times more effective than **vitamin C** and approximately 50 times more effective than **vitamin E** in scavenging free radicals to prevent the **skin** from being damaged. The catechin-based preparation is preferably a proanthanol or a proanthocyanidin, more preferably a proanthanol, and most preferably. . .

SUMM . . . sources. Vitamin B.sub.1, also commonly known as thiamine, aids carbohydrate metabolism, as well as the growth and maintenance of healthy **skin**. Both vitamin B.sub.2 and B.sub.3 are involved in tissue repair. Vitamin B.sub.2, also commonly known as riboflavin, is involved in both the protein and the liquid metabolism necessary to rebuild damaged **skin** tissues. Moreover, **Vitamin B.sub.3** acts as a vasodilator, increasing the blood flow to the **skin** and other tissues. **Vitamin B.sub.3** includes several vitamin B complexes, such as niacin, nicotinic acid, niacinamide, and nicotinamide. Preferably, niacinamide is used in the present. . . several metabolic functions. All of the above vitamin B complexes also enhance the effectiveness of vitamin B.sub.6 in treating the **skin**. Preferably, the B.sub.5 source is pantothenic acid. Each of these vitamin B complexes may be found in the present pharmaceutical. . .

SUMM Also, a **vitamin E** source, which maintains the strength and proper functioning of cells and **skin** tissue membranes, may be included in the present invention. The **vitamin E** source is preferably a sulfate or succinate **vitamin E** complex, more preferably a D-alpha tocopherol acid succinate.

The **vitamin E** source is present in about 1 to 30 weight percent, preferably about 6 to 25 weight percent, and more preferably about 7 to 20 weight percent of the pharmaceutical composition. The unit dose of the **vitamin E** source is typically about 40 mg to 650 mg, preferably about 60 mg to 500 mg, and more preferably about. . .

SUMM These ingredients preferably include at least one amino acid to assist in repairing acne damage to the **skin**. Preferably, two or more amino acids are used. Lysine and proline are the most preferred amino acids and are advantageously. . .

SUMM The magnitude of a prophylactic or therapeutic dose of the composition in the treatment of acne damage to **skin** will vary with the sensitivity of the patient's **skin** and the route of administration. The dose, and perhaps the dose frequency, will also vary according to the age, body. . . mg to 1,600 mg per day. In a preferred form, the invention is used to treat acne and condition the **skin** cells. The oral formulation of the present invention may be used alone or in conjunction with other acne treatments.

DETD

INGREDIENTS	MG PER	PERCENT BY WEIGHT	CHEMICAL OR SCIENTIFIC NAME
Vitamin E Succinate (63.1%)	158.5	13.4%	D-alpha tocopheryl acid succinate
L-Lysine Hcl (80.0%)		13.2%	L-Lysine hydrochloride
Calcium Ascorbate (81.0%)	154.3	13.0%	Calcium ascorbate
Burdock Root. . . Oxide (60.0%)		7.0%	Magnesium oxide
Zinc Ascorbate (15.0%)		2.1%	Zinc ascorbate
Vitamin B.sub.6 (Pyridoxine HCL)	15.1	1.3%	Pyridoxine hydrochloride
(82.7%)			
Grape Seed Extract		1.1%5	Proanthocyanidins
Vitamin B.sub.3 (Niacin)	12.5	1.1%	Niacinamide
Beta Carotene (yields 1,250	10.0	0.9%	Beta carotene
IU per tablet)			
Selenomethionine (0.5%)		0.8%	L-selenomethionine
Biotin (1.0%)		0.6%	7.5

Biotin

Vitamin. . . Riboflavin

Vitamin B.sub.1 (Thiamine)

6.3

0.5%

Thiamine

CHROMEMATE CHROMIUM GTF .TM.

6.3 0.5%

Chromium polynicotinate

(0.2%) Chromium organically bound to nicotinic acid (niacin, **vitamin B.sub.**

3)

Vitamin A Palmitate (yields

2.5

0.2%

Vitamin A

palmitate

1,250 IU per tablet)

Chromium Picolinate (12.0%)

0.1

0.01%

Chromium picolinate

DETD . . . All of the panelists exhibited grade two comedonal/inflammatory acne according to the Acne Grading Scale and were free from any **skin** disorders other than moderate acne. The panelists were instructed to take two tablets in the morning and two in the. . .

CLM What is claimed:

. . . at least one of a zinc compound in an amount greater than 15 mg to about 96 mg or a **Vitamin A** source in an amount sufficient to reduce the redness and blemishes associated with acne; at least one of burdock root yellow dock root, or a catechin-based composition in an amount sufficient to facilitate maintenance of **skin** cells; and a **skin** cell conditioning component comprising a transition metal other than zinc in an amount sufficient to properly regulate the keratin and sebum production of the **skin** cells to inhibit the appearance of acne.

6. The pharmaceutical composition of claim 5, wherein the **vitamin A** source comprises **vitamin A** complexed with an acetate or **palmitate**, the carotenoid component comprises beta-carotene, the vitamin B.sub.6 source comprises a pyridoxine, and the zinc component comprises zinc complexed with. . .

7. The pharmaceutical composition of claim 6, wherein the **vitamin A** source is **vitamin A** **palmitate** present in about 0.005 to 5 weight percent, beta-carotene is present in about 0.1 to 10 weight percent, the pyridoxine. . .

9. The pharmaceutical composition of claim 1, further comprising at least one of a **vitamin C** source, horsetail extract, a vitamin B.sub.1 source, a vitamin B.sub.2 source, a **vitamin B.sub.3** source, a vitamin B.sub.5 source, and a **vitamin E** source, all in an amount sufficient to facilitate maintenance of **skin** cells.

10. The pharmaceutical composition of claim 9, wherein the **vitamin C** source comprises ascorbic acid or ascorbate, the catechin-based composition comprises a proanthanol or proanthocyanidin, the vitamin B.sub.1 source comprises thiamin, the vitamin B.sub.2 source comprises riboflavin, the **vitamin**

B.sub.3 source comprises niacinamide, the vitamin B.sub.5 source comprises pantothenic acid, and the **vitamin E** source comprises a sulfate or succinate **vitamin E** complex.

11. The pharmaceutical composition of claim 10, wherein the **vitamin C** source is calcium ascorbate present in about 1 to 30 weight percent, the burdock root is present in about 1. . . in about 0.05 to 5 weight percent, the thiamin is present in about 0.05 to 5 weight percent and the **vitamin E** source is **vitamin E** succinate present in about 1 to 30 weight percent.

. . . one amino acid component, a magnesium component, a selenium component, and biotin in an amount sufficient to facilitate repair of **skin** damaged by acne.

15. A method for conditioning **skin** cells in a patient which comprises administering: an acne reduction component comprising at least one of a zinc compound or a **Vitamin A** compound; at least one of burdock root, yellow dock root, or a catechin-based composition in an amount sufficient to facilitate maintenance of **skin** cells; and a **skin** cell conditioning component comprising a transition metal other than zinc, said components administered in an amount therapeutically effective to regulate the keratin and sebum production of the **skin** cells and to reduce the redness and blemishes associated with acne.

. . . conjunction with concurrent or subsequent treatment by at least an additional pharmaceutical composition used to treat acne or condition the **skin**.

. . . wherein the additional pharmaceutical composition is: a topical application comprising at least one of: alcohol, benzoyl peroxide, erythromycin, clindamycin, tretinoin, **vitamin E**, and **vitamin A** or its derivatives; or an oral application comprising at least one of: erythromycin, tetracycline, isotretinoin, **vitamin C**, vitamin D, chaparral, dandelion root, licorice root, echinacea, kelp, cayenne, sassafras, elder flowers, pantothenic acid, para-aminobenzoic acid, biotin, choline, inositol, folic acid, calcium, magnesium, potassium and **Vitamin A** derivatives.

L7 ANSWER 14 OF 18 USPATFULL
AN 1999:96033 USPATFULL
TI Methods of regulating **skin** appearance with **vitamin B.sub.3** compound
IN Oblong, John Erich, Cincinnati, OH, United States
Bissett, Donald Lynn, Hamilton, OH, United States
Biedermann, Kimberly Ann, Cincinnati, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5939082 19990817 <--
AI US 1997-834010 19970411 (8)
RLI Continuation-in-part of Ser. No. US 1995-554067, filed on 6 Nov 1995, now patented, Pat. No. US 5833998
PRAI US 1996-16043P 19960423 (60)
US 1996-25242P 19960916 (60)
US 1996-28902P 19961021 (60)
DT Utility
FS Granted

EXNAM Primary Examiner: Venkat, Jyothsna
LREP Little, Darryl C., Allen, George W.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2003
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Methods of regulating **skin** appearance with **vitamin B.sub.3** compound
PI US 5939082 19990817 <--
AB The present invention relates to topical compositions comprising a **vitamin B.sub.3** compound which are useful for regulating **skin** condition, especially for regulating the signs of **skin** aging.
SUMM The present invention relates to topical compositions containing a **vitamin B.sub.3** compound for regulating the condition of **skin**, especially for regulating visible and/or tactile discontinuities in **skin** associated, e.g., with **skin** aging. Preferred compositions contain niacinamide.
SUMM Many personal care products currently available to consumers are directed primarily to improving the health and/or physical appearance of the **skin**. Among these **skin** care products, many are directed to delaying, minimizing or even eliminating **skin** wrinkling and other histological changes typically associated with the aging of **skin** or environmental damage to human **skin**.
SUMM **Skin** is subject to insults by many extrinsic and intrinsic factors. Extrinsic factors include ultraviolet radiation (e.g., from sun exposure), environmental. . . low humidity, harsh surfactants, abrasives, and the like. Intrinsic factors include chronological aging and other biochemical changes from within the **skin**. Whether extrinsic or intrinsic, these factors result in visible signs of **skin** aging and environmental damage, such as wrinkling and other forms of roughness (including increased pore size, flaking and **skin** lines), and other histological changes associated with **skin** aging or damage. To many people, **skin** wrinkles are a reminder of the disappearance of youth. As a result, the elimination of wrinkles has become a booming. . .
SUMM Extrinsic or intrinsic factors may result in the thinning and general degradation of the **skin**. For example, as the **skin** naturally ages, there is a reduction in the cells and blood vessels that supply the **skin**. There is also a flattening of the dermal-epidermal junction which results in weaker mechanical resistance of this junction. See, for example, Oikarinen, "The Aging of **Skin**: Chronoaging Versus Photoaging," Photodermatol. Photoimmunol. Photomed., vol. 7, pp. 3-4, 1990, which is incorporated by reference herein in its entirety.
SUMM It has now been found that **vitamin B.sub.3** compounds, including niacinamide, provide benefits in regulating **skin** condition previously unrecognized in the art of which the present inventors are aware. For example, topical niacinamide can regulate the signs of **skin** aging, e.g., reduce or efface the visibility of the fine lines, wrinkles, and other forms of uneven or rough surface texture associated with aged or photodamaged **skin**. It has also now been found that topical compositions containing a **vitamin B.sub.3** compound and a retinoid provide benefits in regulating **skin** condition previously unrecognized in the art of which the present inventors are aware. For example, such compositions enable the regulation of signs of **skin** aging with decreased potential for retinoid dermatitis. In addition, the **vitamin B.sub.3** compound in combination with certain retinoids

synergistically regulates signs of **skin** aging, especially visible and/or tactile discontinuities in **skin** texture associated with aged **skin**, including fine lines and wrinkles.

SUMM It is therefore an object of the present invention to provide topical compositions for prophylactically and/or therapeutically regulating mammalian **skin** condition (especially of human **skin**, more especially facial **skin**), containing a **vitamin B.sub.3** compound, especially niacinamide.

SUMM It is another object of the present invention to provide topical compositions for prophylactically and/or therapeutically regulating signs of mammalian **skin** aging, containing a **vitamin B.sub.3** compound, especially niacinamide.

SUMM . . . object of the present invention to provide topical compositions for prophylactically and/or therapeutically regulating visible and/or tactile discontinuities in mammalian **skin** texture, including fine lines, wrinkles, enlarged pores, roughness and other **skin** texture discontinuities associated with aged **skin**, containing a **vitamin B.sub.3** compound, especially niacinamide.

SUMM The present invention relates to regulation of **skin** condition involving the topical application of a composition containing a **vitamin B.sub.3** compound, especially niacinamide. The present invention also relates to regulation of **skin** condition involving topical application of a composition containing a **vitamin B.sub.3** compound, especially niacinamide, and a retinoid. The invention especially relates to regulation of signs of **skin** aging, more especially regulating visible and/or tactile discontinuities in mammalian **skin** texture, including discontinuities associated with aged **skin**, involving the topical application of such compositions. The present invention relates to both prophylactic and therapeutic regulation of **skin** condition.

SUMM In preferred embodiments, the **vitamin B.sub.3** compound is substantially free of the salt form and is uncomplexed, the **vitamin B.sub.3** compound is niacinamide, and the carrier contains a hydrophilic diluent.

SUMM . . . application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the **skin**.

SUMM . . . as used herein, means that the compositions or components thereof so described are suitable for use in contact with human **skin** without undue toxicity, incompatibility, instability, allergic response, and the like.

SUMM . . . used herein means an amount of a compound or composition sufficient to significantly induce a positive benefit, preferably a positive **skin** appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to. . .

SUMM The compositions of the present invention are useful for topical application and for regulating **skin** condition, including visible and/or tactile discontinuities in **skin** (especially the **skin** surface; such discontinuities are generally undesired). Such discontinuities may be induced or caused by internal and/or external factors, and include the signs of **skin** aging described herein. "Regulating **skin** condition" includes prophylactically regulating and/or therapeutically regulating **skin** condition, including visible and/or tactile discontinuities in **skin**. As used herein, prophylactically regulating **skin** condition includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in **skin**. As used herein, therapeutically regulating **skin** condition includes ameliorating, e.g., diminishing, minimizing and/or effacing,

discontinuities in **skin**. Regulating **skin** condition involves improving **skin** appearance and/or feel.

SUMM The compositions of the present invention are useful for regulating signs of **skin** aging, more especially visible and/or tactile discontinuities in **skin** texture associated with aging. "Regulating the signs of **skin** aging" includes prophylactically regulating and/or therapeutically regulating one or more of such signs (similarly, regulating a given sign of **skin** aging, e.g., lines, wrinkles or pores, includes prophylactically regulating and/or therapeutically regulating that sign). As used herein, prophylactically regulating such signs includes delaying, minimizing and/or preventing signs of **skin** aging. As used herein, therapeutically regulating such signs includes ameliorating, e.g., diminishing, minimizing and/or effacing signs of **skin** aging.

SUMM "Signs of **skin** aging" include, but are not limited to, all outward visibly and tactilely perceptible manifestations as well as any other macro or micro effects due to **skin** aging. Such signs may be induced or caused by intrinsic factors or extrinsic factors, e.g., chronological aging and/or environmental damage.. . . not limited to, the development of textural discontinuities such as wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, **skin** lines, crevices, bumps, large pores (e.g., associated with adnexal structures such as sweat gland ducts, sebaceous glands, or hair follicles), scaliness, flakiness and/or other forms of **skin** unevenness or roughness, loss of **skin** elasticity (loss and/or inactivation of functional **skin** elastin), sagging (including puffiness in the eye area and jowls), loss of **skin** firmness, loss of **skin** tightness, loss of **skin** recoil from deformation, discoloration (including undereye circles), blotching, sallowness, hyperpigmented **skin** regions such as age spots and freckles, keratoses, abnormal differentiation, hyperkeratinization, elastosis, collagen breakdown, and other histological changes in the stratum corneum, dermis, epidermis, the **skin** vascular system (e.g., telangiectasia or spider vessels), and underlying tissues, especially those proximate to the **skin**.

SUMM . . . to be understood that the present invention is not to be limited to regulation of the above mentioned "signs of **skin** aging" which arise due to mechanisms associated with **skin** aging, but is intended to include regulation of said signs irrespective of the mechanism of origin. As used herein, "regulating **skin** condition" is intended to include regulation of such signs irrespective of the mechanism of origin.

SUMM The present invention is especially useful for therapeutically regulating visible and/or tactile discontinuities in mammalian **skin** texture, including texture discontinuities associated with **skin** aging. As used herein, therapeutically regulating such discontinuities includes ameliorating, e.g., diminishing, minimizing and/or effacing visible and/or tactile discontinuities in the texture of mammalian **skin**, to thereby provide improved **skin** appearance and/or feel, e.g., a smoother, more even appearance and/or feel. Such visible and/or tactile discontinuities in **skin** texture include crevices, bumps, pores, fine lines, wrinkles, scales, flakes and/or other forms of textural unevenness or roughness associated with **skin** aging. For example, the length, depth, and/or other dimension of lines and/or wrinkles are decreased, the apparent diameter of pores decreases, or the apparent height of tissue immediately proximate to pore openings approaches that of the interadnexal **skin**.

SUMM The present invention is also especially useful for prophylactically regulating visible and/or tactile discontinuities in mammalian **skin** texture, including texture discontinuities associated with **skin** aging. As used herein, prophylactically regulating such

discontinuities includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in the texture of mammalian **skin**, to thereby provide improved **skin** appearance and/or feel, e.g., a smoother, more even appearance and/or feel.

SUMM The compositions of the present invention are also useful for promoting exfoliation of the **skin**. Without intending to be bound or limited by theory, it is believed that the compositions containing the **vitamin B.sub.3** compound, particularly niacinamide, strengthen the energy state of cells regulating exfoliation, resulting in normalization of epidermal differentiation and keratinization.

SUMM **Vitamin B.sub.3** Component

SUMM The compositions of the present invention comprise a safe and effective amount of a **vitamin B.sub.3** compound. The compositions of the present invention preferably comprise from about 0.01% to about 50%, more preferably from about 0.1%. . . and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the **vitamin B.sub.3** compound.

SUMM As used herein, "**vitamin B.sub.3** compound" means a compound having the formula: ##STR1## wherein R is --CONH.sub.2 (i.e., niacinamide), --COOH (i.e., nicotinic acid) or --CH.sub.2. . .

SUMM Exemplary derivatives of the foregoing **vitamin B.sub.3** compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids,. . .

SUMM . . . As used herein, "non-vasodilating" means that the ester does not commonly yield a visible flushing response after application to the **skin** in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds. . .

SUMM Other derivatives of the **vitamin B.sub.3** compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of. . .

SUMM . . . esters of the carboxylic acids salicylic acid, acetic acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of **vitamin B.sub.3** compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methylnicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid,. . .

SUMM Examples of the above **vitamin B.sub.3** compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical. . .

SUMM One or more **vitamin B.sub.3** compounds may be used herein. Preferred **vitamin B.sub.3** compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

SUMM . . . and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating **skin** condition described herein.

SUMM Salts of the **vitamin B.sub.3** compound are also useful herein. Nonlimiting examples of salts of the **vitamin B.sub.3** compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide,. . . e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the **vitamin B.sub.3**

compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic. . .

SUMM In a preferred embodiment, the ring nitrogen of the **vitamin B.sub.3** compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the **skin** becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the **vitamin B.sub.3** compound is essentially uncomplexed. Therefore, if the composition contains the **vitamin B.sub.3** compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the **skin**. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility. . .

SUMM More preferably the **vitamin B.sub.3** compound is substantially uncomplexed in the composition prior to delivery to the **skin**. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the **vitamin B.sub.3** compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the **vitamin B.sub.3** compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill. . .

SUMM Thus, in a preferred embodiment, the **vitamin B.sub.3** compound contains a limited amount of the salt form and is more preferably substantially free of salts of a **vitamin B.sub.3** compound. Preferably the **vitamin B.sub.3** compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The **vitamin B.sub.3** compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about. . .

SUMM The **vitamin B.sub.3** compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The **vitamin B.sub.3** compound is preferably substantially pure, more preferably essentially pure.

SUMM The compositions of the present invention comprise a dermatologically acceptable carrier within which the **vitamin B.sub.3** compound is incorporated to enable the **vitamin B.sub.3** compound and optional other actives to be delivered to the **skin** at an appropriate concentration. The carrier can thus act as a diluent, dispersant, solvent, or the like for the active(s). . .

SUMM Preferred carriers contain a dermatologically acceptable, hydrophilic diluent. As used herein, "diluent" includes materials in which the **vitamin B.sub.3** compound can be dispersed, dissolved, or otherwise incorporated. Hydrophilic diluents include water, organic hydrophilic diluents such as lower monovalent alcohols. . . is a preferred diluent. The composition preferably comprises from about 80% to about 99.99% of the hydrophilic diluent and the **vitamin B.sub.3** compound in the above described amounts.

SUMM . . . Solutions useful in the subject invention preferably contain from about 80% to about 99.99% of the hydrophilic diluent and the **vitamin B.sub.3** compound in the above described amounts.

SUMM . . . Science and Technology, 2nd Edition, Vol. 2, pp. 443-465 (1972), incorporated herein by reference. Aerosols are typically applied to the **skin** as a spray-on product.

SUMM . . . primarily into either the water or oil/silicone phase, depending on the water solubility/dispersibility of the component in the composition. Preferred **vitamin B.sub.** **3** compounds distribute primarily into the aqueous phase. Oil-in-water emulsions are especially preferred.

SUMM The emulsion may also contain an anti-foaming agent to minimize foaming upon application to the **skin**. Anti-foaming agents include high molecular weight silicones and other materials well known in the art for such use.

SUMM . . . refers to a material useful for the prevention or relief of dryness, as well as for the protection of the **skin**. A wide variety of suitable emollients are known and may be used herein. Sagarin, Cosmetics Science and Technology, 2nd Edition,. . .

SUMM . . . about 10%, of emollient; from about 50% to about 90%, preferably from about 60% to about 80%, water; and the **vitamin B.sub.3** compound in the above described amounts. A cream typically comprises from about 5% to about 50%, preferably from about 10%. . . about 20%, of emollient; from about 45% to about 85%, preferably from about 50% to about 75%, water; and the **vitamin B.sub.3** compound in the above described amounts.

SUMM . . . about 2% to about 10% of an emollient; from about 0.1% to about 2% of a thickening agent; and the **vitamin B.** **sub.3** compound in the above described amount.

SUMM . . . for cleansing ("cleansers") are formulated with a suitable carrier, e.g., as described above, and preferably contain, in addition to the **vitamin B.sub.3** compound in the above described amounts, from about 1% to about 90%, more preferably from about 5% to about 10%,. . .

SUMM . . . mousses. Toilet bars are most preferred since this is the form of cleansing agent most commonly used to wash the **skin**. Rinse-off cleansing compositions, such as shampoos, require a delivery system adequate to deposit sufficient levels of actives on the **skin** and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure of such delivery. . .

SUMM As used herein, the term "foundation" refers to a liquid, semi-liquid, semi-solid, or solid **skin** cosmetic which includes, but is not limited to lotions, creams, gels, pastes, cakes, and the like. Typically the foundation is used over a large area of the **skin**, such as over the face, to provide a particular look. Foundations are typically used to provide an adherent base for color cosmetics such as rouge, blusher, powder and the like, and tend to hide **skin** imperfections and impart a smooth, even appearance to the **skin** . Foundations of the present invention include a dermatologically acceptable carrier for the **vitamin B.sub.** **3** compound and may include conventional ingredients such as oils, colorants, pigments, emollients, fragrances, waxes, stabilizers, and the like. Exemplary carriers. . .

SUMM . . . or other use benefits associated with the compositions of the present invention. Any optional ingredients should be compatible with the **vitamin B.sub.3** compound such that its activity does not decrease unacceptably, preferably not to any significant extent, over a useful period (preferably at least about two years under normal storage conditions). For example, strong oxidizing agents may be incompatible with the **vitamin** **B.sub.3** compound such that such agents are preferably avoided. Optional components may be dispersed, dissolved or the like in the carrier. . .

SUMM . . . additives, cosmetic biocides, denaturants, cosmetic astringents, drug astringents, external analgesics, film formers, humectants, opacifying agents, fragrances, pigments, colorings, essential oils, **skin** sensates, emollients, **skin** soothing agents, **skin** healing agents, pH adjusters, plasticizers, preservatives, preservative enhancers, propellants, reducing agents, additional **skin**-conditioning agents, **skin** penetration enhancing agents, **skin** protectants, solvents, suspending agents, emulsifiers, thickening agents, solubilizing agents, sunscreens, sunblocks, ultraviolet light absorbers or scattering agents, sunless tanning agents,. . .

SUMM It has been found that certain compounds may negatively impact the **skin** appearance benefits otherwise provided by the **vitamin B.sub.3** compound. Such compounds include ascorbic acid and N-acetyl cysteine. Without intending to be bound or limited by theory, it is believed that these compounds may form large complexes, e.g., salts, with the **vitamin B.sub.3** compound which reduce the availability of the **vitamin B.sub.3** compound to the **skin**. Such complexes are believed to have a relatively high molecular weight which decreases their availability to the **skin**. Therefore, in one embodiment of the invention, the compositions do not contain these compounds or compounds which are capable of forming similarly large complexes with the **vitamin B.sub.3** compound. In another embodiment, where the composition contains these compounds or compounds which are capable of forming large complexes with the **vitamin B.sub.3** compound, one or more of the approaches previously described herein for minimizing or preventing the formation of undesirable complexes are. . .

SUMM For example, the impact of such compounds on the efficacy of the **vitamin B.sub.3** compound decreases with a decrease in pH such that pH adjustments can be employed to minimize or obviate such effects.. . .

SUMM . . . 0.1% to about 10%, more preferably from about 0.5% to about 5%, of the composition. The anti-inflammatory agent enhances the **skin** appearance benefits of the present invention, e.g., such agents contribute to a more uniform and acceptable **skin** tone or color. The exact amount of anti-inflammatory agent to be used in the compositions will depend on the particular. . .

SUMM In a preferred embodiment, the compositions of the present invention also contain a retinoid. The **vitamin B.sub.3** compound and retinoid provide unexpected benefits in regulating **skin** condition, especially in therapeutically regulating signs of **skin** aging, more especially wrinkles, lines, and pores. Without intending to be bound or otherwise limited by theory, it is believed that the **vitamin B.sub.3** compound increases the conversion of certain retinoids to trans-retinoic acid, which is believed to be the biologically active form of the retinoid, to provide synergistic regulation of **skin** condition (namely, increased conversion for retinol, retinol esters, and retinal). In addition, the **vitamin B.sub.3** compound unexpectedly mitigates redness, inflammation, dermatitis and the like which may otherwise be associated with topical application of retinoid (often referred to, and hereinafter alternatively referred to as "retinoid dermatitis"). Furthermore, the combined **vitamin B.sub.3** compound and retinoid tend to increase the amount and activity of thioredoxin, which tends to increase collagen expression levels via. . . AP-1. Therefore, the present invention enables reduced active levels, and therefore reduced potential for retinoid dermatitis, while retaining significant positive **skin** conditioning benefits. In

addition, higher levels of retinoid may still be used to obtain greater **skin** conditioning efficacy, without undesirable retinoid dermatitis occurring.

SUMM As used herein, "retinoid" includes all natural and/or synthetic analogs of **Vitamin A** or retinol-like compounds which possess the biological activity of **Vitamin A** in the **skin** as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably retinol, retinol esters (e.g., C.sub.2 -C.sub.22 alkyl esters of retinol, including retinyl **palmitate**, retinyl acetate, retinyl proprionate), retinal, and/or retinoic acid (including all-trans retinoic acid and/or 13-cis-retinoic acid), more preferably retinoids other than. . . adapalene {6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid}, and tazarotene (ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)-ethynyl]nicotinate). One or more retinoids may be used herein. Preferred retinoids are retinol, retinyl **palmitate**, retinyl acetate, retinyl proprionate, retinal and combinations thereof. More preferred are retinol and retinyl **palmitate**.

SUMM . . . contain a safe and effective amount of the retinoid, such that the resultant composition is safe and effective for regulating **skin** condition, preferably for regulating visible and/or tactile discontinuities in **skin**, more preferably for regulating signs of **skin** aging, even more preferably for regulating visible and/or tactile discontinuities in **skin** texture associated with **skin** aging. The compositions preferably contain from or about 0.005% to or about 2%, more preferably 0.01% to or about 2%,. . . used in an amount of from or about 0.01% to or about 2%. When the composition contains a retinoid, the **vitamin B**. **sub.3** compound is preferably used in an amount of from or about 0.1% to or about 10%, more preferably from or. . .

SUMM . . . by interfering with the action of androgens at their target organs. The target organ for the subject invention is mammalian **skin**. Exemplary antiandrogens include pregnenalone (and its derivatives), hops extract, oxygenated alkyl substituted bicyclo alkanes (e.g., ethoxyhexyl-bicyclo octanones such as marketed. . .

SUMM An agent may also be added to any of the compositions useful in the subject invention to improve the **skin** substantivity of those compositions, particularly to enhance their resistance to being washed off by water, or rubbed off. A preferred. . .

SUMM . . . which can cause increased scaling or texture changes in the stratum corneum and against other environmental agents which can cause **skin** damage.

SUMM Anti-oxidants/radical scavengers such as ascorbic acid (**vitamin C**) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate), tocopherol (**vitamin E**), tocopherol sorbate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under the tradename. . . acid and its salts, lycine pidolate, arginine pilolate, nordihydroguaiaretic acid, bioflavonoids, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape **skin**/seed extracts, melanin, and rosemary extracts may be used. Preferred anti-oxidants/radical scavengers are selected from tocopherol sorbate and other esters of. . .

SUMM . . . of a chelating agent is especially useful for providing protection against UV radiation which can contribute to excessive scaling or **skin** texture changes and against other environmental agents which can cause **skin** damage.

SUMM . . . about 5%, also preferably from about 0.5% to about 2%. Salicylic acid is preferred. The organic hydroxy acids enhance the **skin** appearance benefits of the present invention. For example, the organic hydroxy acids tend to improve the texture of the

skin.

SUMM . . . about 0.2% to about 5%, also preferably from about 0.5% to about 4% of the composition. Desquamation agents enhance the **skin** appearance benefits of the present invention. For example, the desquamation agents tend to improve the texture of the **skin** (e.g., smoothness). A variety of desquamation agents are known in the art and are suitable for use herein, including but. . .

SUMM K. **Skin** Lightening Agents

SUMM The compositions of the present invention may comprise a **skin** lightening agent. When used, the compositions preferably comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%, of a **skin** lightening agent. Suitable **skin** lightening agents include those known in the art, including kojic acid, arbutin, ascorbic acid and derivatives thereof, e.g., magnesium ascorbyl phosphate. **Skin** lightening agents suitable for use herein also include those described in copending patent application Ser. No. 08/479,935, filed on Jun.. . .

SUMM M. Humectants, Moisturizers, and **Skin** Conditioners

SUMM The compositions of the present invention may further comprise a humectant, moisturizing agent or other **skin** conditioning agent. A variety of these materials can be employed and each can be present at a level of from. . .

SUMM . . . fungi, by-products of microorganisms), including those known in the topical personal care art. Preferred extracts are those which enhance the **skin** appearance benefits of the present invention, and which are preferably used in a safe and effective amount, more preferably an. . .

SUMM Other examples of additional components useful herein include the following: water-soluble vitamins and derivatives thereof [e.g., **vitamin C**]; polyethyleneglycols and polypropyleneglycols; polymers for aiding the film-forming properties and substantivity of the composition (such as a copolymer of eicosene. . .

SUMM Also useful herein are aesthetic components such as fragrances, pigments, colorings, essential oils, **skin** sensates, astringents, **skin** soothing agents, **skin** healing agents and the like, nonlimiting examples of these aesthetic components include clove oil, menthol, camphor, eucalyptus oil, eugenol, menthyl. . .

SUMM Methods for Regulating **Skin** Condition

SUMM The compositions of the present invention are useful for regulating mammalian **skin** condition (especially human **skin**, more especially human facial **skin**), including visible and/or tactile discontinuities in **skin**, signs of **skin** aging, and visible and/or tactile discontinuities in **skin** associated with **skin** aging (including fine lines, wrinkles, large pores, surface roughness and other texture discontinuities associated with aged **skin**). Such regulation includes prophylactic and therapeutic regulation.

SUMM Regulating **skin** condition involves topically applying to the **skin** a safe and effective amount of a composition of the present invention. The amount of the composition which is applied, the frequency of application and the period of use will vary widely depending upon the level of **vitamin B.sub.3** compound and/or other components of a given composition and the level of regulation desired, e.g., in light of the level of **skin** aging present in the subject and the rate of further **skin** aging.

SUMM In a preferred embodiment, the composition is chronically applied to the **skin**. By "chronic topical application" is meant continued topical application of the composition over an extended period during the subject's lifetime,. . .

SUMM A wide range of quantities of the compositions of the present invention can be employed to provide a **skin** appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm.sup.2 **skin**, from about 0.1 mg/cm.sup.2 to about 10 mg/cm.sup.2. A particularly useful application amount is about 2 mg/cm.sup.2.

SUMM Regulating **skin** condition is preferably practiced by applying a composition in the form of a **skin** lotion, cream, cosmetic, or the like which is intended to be left on the **skin** for some esthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition). After applying the composition to the **skin**, it is preferably left on the **skin** for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at. . .

DETD A **skin** cream is prepared by conventional methods from the following components.

DETD Apply the composition to a subject's wrinkled, aged, or photodamaged facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** once or twice daily for a period of at least 3-6 months to reduce fine lines and wrinkles and improve **skin** surface texture.

DETD Apply the resulting composition to a subjects wrinkled, aged, or photodamaged facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** once or twice daily for a period of at least 3-6 months to reduce fine lines and wrinkles and improve **skin** surface texture.

DETD A **skin** cream is prepared by conventional methods from the following components.

DETD Apply the composition to a subject's wrinkled, aged, or photodamaged facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** once or twice daily for a period of at least 3-6 months to reduce fine lines and wrinkles and improve **skin** surface texture.

DETD A **skin** cream is prepared by conventional methods from the following components.

DETD Apply the composition to a subject's wrinkled, intrinsically aged, or photodamaged facial **skin** at the rate of 2 mg composition/cm.sup.2 **skin** once or twice daily for a period of at least 3-6 months to improve **skin** surface texture, including diminishing fine lines and wrinkles.

DETD An alternative **skin** cream having reduced retinol levels can be prepared in the same manner from the above components wherein the retinol is. . .

CLM What is claimed is:

1. A method of regulating mammalian **skin** pore size, comprising applying to the **skin** of a mammal a safe and effective amount of a composition comprising: (a) a safe and effective amount of a **vitamin B.sub.3** compound selected from the group consisting of niacinamide, tocopherol nicotinate, and combinations thereof; and (b) a carrier for said **vitamin B.sub.3** compound.

2. The method of claim 1 wherein said **vitamin B. sub.3** compound is niacinamide.

3. A method of regulating mammalian **skin** pore size, comprising applying to the **skin** of a mammal a safe and effective amount of a composition comprising: (a) a safe and effective amount of a **vitamin B.sub.3** compound selected from the group consisting of niacinamide, tocopherol nicotinate, and combinations thereof; (b) a second active selected from the. . . consisting of retinol, retinol esters, retinal, retinoic acid,

tocopheryl-retinoate, adapalene, tazarotene and combinations thereof; and (c) a carrier for said **vitamin B.sub.** **3** compound.

4. The method of claim 3 wherein said retinoid is selected from the group consisting of retinol, retinyl **palmitate**, retinyl acetate, retinyl proprionate, retinal and combinations thereof.

5. The method of claim 4 wherein said retinoid is selected from the group consisting of retinol, retinyl **palmitate**, and combinations thereof.

L7 ANSWER 15 OF 18 USPATFULL
AN 1998:108425 USPATFULL
TI Pharmaceutical compositions and methods for improving wrinkles and other **skin** conditions
IN Murad, Howard, 4316 Marina City Dr., Marina del Rey, CA, United States 90292
PI US 5804594 19980908 <--
AI US 1997-787358 19970122 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: MacMillan, Keith D.
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1066
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Pharmaceutical compositions and methods for improving wrinkles and other **skin** conditions
PI US 5804594 19980908 <--
AB This application relates to a pharmaceutical composition for the prevention and treatment of **skin** conditions in a patient having a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**, a primary antioxidant component in an amount sufficient to substantially inhibit the formation of collagenase and elastase, at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**, and at least one transition metal component in an amount effective to bind collagen and elastic fibers and rebuild **skin** . In one preferred form, the composition further includes a catechin-based preparation, a glucosamine or a pharmaceutically acceptable salt or ester. . . a chondroitin or a pharmaceutically acceptable salt or ester thereof. In a more preferred form, the invention further includes a **vitamin E** source, a cysteine source, a **vitamin B.sub.3** source, quercetin dihydrate, pyridoxal 5 phosphate-Co B.sub.6, a methionine source, and a **vitamin A** source. The invention further relates to a method for the prevention or treatment of **skin** conditions by administering the pharmaceutical composition in an amount therapeutically effective to modify the thickness of the **skin** to prevent or treat at least one **skin** condition.
SUMM . . . well as methods, to supplement collagen and elastic tissues and thicken the dermis for the treatment of wrinkles and other **skin** conditions.
SUMM Human **skin** is a composite material of the epidermis and the dermis. The topmost part of the epidermis is the stratum corneum. This layer is the stiffest layer of the **skin**, as well as the one most affected by the surrounding environment. Below the stratum corneum is the internal portion of. . . the dermis is the papillary dermis,

which is made of relatively loose connective tissues that define the micro-relief of the **skin**. The reticular dermis, disposed beneath the papillary dermis, is tight, connective tissue that is spatially organized. The reticular dermis is. . .

SUMM The principal functions of the **skin** include protection, excretion, secretion, absorption, thermoregulation, pigmentogenesis, accumulation, sensory perception, and regulation of immunological processes. These functions are detrimentally affected by the structural changes in the **skin** due to aging and excessive sun exposure. The physiological changes associated with **skin** aging include impairment of the barrier function and decreased turnover of epidermal cells, for example. [Cerimele, D., et al., Br.. . .

SUMM The mechanical properties of the **skin**, such as elasticity, are controlled by the density and geometry of the network of collagen and elastic fiber tissue therein. Damaged collagen and elastin lose their contractile properties, resulting in **skin** wrinkling and **skin** surface roughness. As the **skin** ages or becomes unhealthy, it acquires sags, stretch marks, bumps, bruises or wrinkles, it roughens, and it has reduced ability to synthesize Vitamin D. Aged **skin** also becomes thinner and has a flattened dermoepidermal interface because of the alterations in collagen, elastin, and glycosaminoglycans. [Fenske, N.. . .

SUMM A variety of vitamins and minerals have in individually been administered to treat certain **skin** and other problems that occur when the patient has a deficiency of that vitamin or mineral. **Vitamin A**, for example, assists in the treatment of acne and to facilitate wound healing; **vitamin C** (ascorbic acid) assists in the prevention of **skin** bruising and wound healing; **vitamin E** is an antioxidant; and copper assists in the treatment of elastic tissue defects. [Neldner, K. H., Amer. Acad. Derm. Annl. Mtg., Wash D.C., Dec. 6, 1993]. Topical use of **vitamin C** is also believed to ward off sun damage, reduce breakdown of connective tissues, and possibly promote collagen synthesis. [Dial, W., Medical World News, p. 12, March 1991]. **Vitamin E** is used topically as an anti-inflammatory agent, for enhancement of **skin** moisturization, for UV-ray protection of cells, and for retardation of premature **skin** aging.

SUMM . . . metabolism of glycosaminoglycans under the influence of herbal and other anti-inflammatory agents has been examined by measuring glycosaminoglycans in the **skin**, liver, kidney, and spleen after administration of several compounds. [Reddy, G. K., et al., Biochem. Pharmacology, 38(20):3527-3534 (1989)].

SUMM . . . a patient, various of the above ingredients have been combined to form pharmaceuticals designed to prevent and treat certain cellular, **skin**, and other conditions. For example, U.S. Pat. No. 3,773,930 discloses a low residue, dietary composition having at least one amino. . .

SUMM U.S. Pat. No. 4,414,202 discloses a composition for the treatment of **skin** wounds with a buffered salt solution having a pH between 6 to 7.8 and administering a starch hydrolysate compound, and. . .

SUMM U.S. Pat. No. 4,424,232 discloses a topical composition for the treatment of herpes simplex, cold sores, lesions, and other painful **skin** conditions including L-lysine, gibberellic acid, and urea in an inert carrier having water. The composition may also include L-ascorbic acid,. . .

SUMM U.S. Pat. No. 5,198,465 discloses a composition for treating precursor deficiencies in the synthesis of collagen with proline, glycine, lysine, **vitamin C**, and one or more compounds selected from a-ketoglutaric acid, methionine, cysteine, cystine, valine, and pharmaceutically acceptable diluents and excipients.

SUMM . . . complexes; an enzyme producer such as an amino acid like

glutamic acid; an herbal antispasmodic substance like Valerian root; and **vitamin C**.

SUMM U.S. Pat. No. 5,415,875 discloses a method of suppressing formation of lipid peroxide and removing peroxide by applying to the **skin** a decomposed product of shell membrane and tocopherol and derivatives. Lysine, proline, **Vitamin C**, for examples, are listed among a vast genus of optional additives.

SUMM The above references, however, do not teach pharmaceutical compositions or methods for improving **skin** wrinkles along with other conditions, such as **skin** elasticity and softness. Thus, it is desired to find a pharmaceutical composition and a method for the prevention and treatment of wrinkles and other **skin** conditions. The present invention advantageously provides pharmaceutical compositions, as well as methods of treatment comprising the administration of such compositions, to repair **skin** for the prevention and treatment of wrinkles and other **skin** disorders.

SUMM The present invention relates to a pharmaceutical composition for the prevention and treatment of **skin** conditions in a patient having a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**, a primary antioxidant component in an amount sufficient to substantially inhibit the activity of collagenase and elastase, at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**, and at least one transition metal component in an amount effective to bind collagen and elastic fibers and rebuild **skin** .

SUMM In another preferred embodiment, the composition further includes a **vitamin E** source, a cysteine source, a **vitamin B.sub.3** source, quercetin dihydrate, pyridoxal 5 phosphate-Co B.sub.6, a methionine source, and a **vitamin A** source. In a more preferred embodiment, the **vitamin E** is D-alpha tocopheryl acid succinate present in about 1 to 15 weight percent, the **vitamin B. sub.3** is niacinamide present in about 0.5 to 15 weight percent, the **vitamin A** is **vitamin A palmitate** present in about 0.1 to 5 weight percent, the cysteine is N-acetyl cysteine present in about 1 to 10 weight. . .

SUMM The invention further relates to a method for the prevention or treatment of **skin** conditions, wherein the **skin** has a thickness of dermis and collagen, which includes administering the pharmaceutical composition above in an amount therapeutically effective to modify the thickness of the **skin** to prevent or treat at least one **skin** condition.

SUMM In one embodiment according to the invention, the **skin** condition treated is at least one of wrinkles, fine lines, thinning, reduced **skin** elasticity, reduced **skin** moisture, spider veins, senile purpura, sun damaged **skin**, aging **skin**, or rough **skin**. In another embodiment, the composition is administered orally. In a preferred embodiment, the composition is administered as a tablet or. . .

SUMM . . . conjunction with concurrent or subsequent treatment by at least one additional pharmaceutical composition for the prevention or treatment of a **skin** condition.

SUMM A formulation for the reduction of wrinkles and the improvement of other **skin** conditions, such as increased **skin** elasticity and **skin** softness, has now been discovered. Moreover, the prevention or treatment of unhealthy **skin**, such as aged **skin** or **skin** overexposed to sunlight, may advantageously be accomplished by the administration of the pharmaceutical composition of the present invention to a. . . pharmaceutical composition includes the combination of a number of different components which interact to provide the desired improvements to the **skin**.

SUMM The advantageous pharmaceutical composition of the present invention prevents and improves **skin** conditions by using a sufficient amount of at least one sugar compound which is converted into glycosaminoglycans in the bloodstream,. . . supplementing collagen and elastic tissues. A thicker dermis desirably reduces the wrinkling and lines that occur when areas of the **skin** become thin. Various amino acids such as lysine, proline and cysteine assist in the thickening of the dermis, supplementing of collagen and elastic tissues and, consequently, reduction of wrinkles and other **skin** conditions. Additionally, antioxidants, such as **vitamin C**, inhibit collagenase and elastase, enzymes that break down collagen and elastic tissues. These antioxidants assist in the prevention of additional wrinkles and facilitate the healing of **skin** tissues. Finally, transition metal components are included to bind collagen fibers and inhibit elastase, an enzyme that also breaks down. . .

SUMM The pharmaceutical composition includes a primary antioxidant, which typically is a **vitamin C** source and preferably is ascorbic acid, or a pharmaceutically acceptable salt or ester thereof, and more preferably is ascorbyl **palmitate**, dipalmitate L-ascorbate, sodium L-ascorbate-2-sulfate, or an ascorbic salt, such as sodium, potassium, or calcium ascorbate, or mixtures thereof. When oral formulations of the pharmaceutical composition are used, it is preferred that a non-acidic form of **vitamin C** be used to reduce the stomach irritation that may occur when using an acidic form. The **vitamin C** source is present in the pharmaceutical composition in about 5 to 50 weight percent, preferably about 7 to 40 weight percent, and more preferably about 10 to 25 weight percent. A unit dose of this primary **vitamin C** source is typically about 40 mg to 400 mg, preferably about 60 mg to 300 mg, and more preferably about 80 to 150 mg. **Vitamin C** is also approved by the FDA and has wide consumer acceptance, so that it can be used in amounts as. . .

SUMM The pharmaceutical composition also includes at least one amino acid to assist in thickening the **skin**. Preferably two or more amino acids are used in combination. Either the L- or D- forms of amino acids are. . .

SUMM . . . or more transition metal compounds are included in an amount effective to bind collagen and elastic tissue to rebuild the **skin**. Certain transition metal compounds inhibit the elastase enzyme to inhibit collagen and elastic tissue breakdown. Preferred transition metals include zinc,. . .

SUMM . . . assist in binding collagen and elastic fibers, which both assists in the prevention of wrinkles and the rebuilding of wrinkled **skin**. The zinc component may be any zinc compound or pharmaceutically acceptable salt thereof, but more preferably is a zinc complexed. . .

SUMM . . . or pharmaceutically acceptable salt thereof, but more preferably is a manganese component which is at least partially complexed with a **vitamin C** source, and most preferably is manganese ascorbate or manganese ascorbic acid, wherein the manganese is typically present in about 5 to 20 weight percent of the complex. When complexed with **vitamin C**, this **vitamin C** source may be included in the overall percentage of **vitamin C** in the pharmaceutical composition. The manganese component is present in about 1 to 10 weight percent, more preferably about 2. . .

SUMM The catechin-based preparation, similar to **vitamin C**, inhibits elastase and collagenase, which is another enzyme that attacks elastic tissue and collagen. The catechin-based preparation is preferably a. . .

SUMM . . . 90 weight percent of the salt. The glucosamine content of this

component contributes to the formation of glycosoaminoglycans in the **skin**. The chondroitin component preferably is present as a sulfate or succinate, and more preferably is chondroitin sulfate, wherein the chondroitin. . .

SUMM In a more preferred form, several optional additives are included in the pharmaceutical composition, such as a **vitamin E** source, a **vitamin B.sub.3** source, quercetin powder, pyridoxal 5 phosphate-Co B.sub.6, and a **vitamin A** source. The **vitamin E** preferably is a sulfate or succinate **vitamin E** complex, and more preferably is D-alpha tocopheryl acid succinate. The **vitamin E** source is present in about 1 to 15 weight percent, preferably about 2 to 12 weight percent, and more preferably. . . 10 weight percent of the composition. In any event, no more than 1,500 IU should be ingested per day, as **Vitamin E** becomes toxic at higher doses. The **vitamin B. sub.3** source preferably is niacinamide, and the source is present in about 0.5 to 15 weight percent, preferably about 1 to 12 weight percent, and more preferably about 1.5 to 10 weight percent of the composition. The **vitamin A** source preferably is **vitamin A palmitate,** and the source is present in about 0.1 to 5 weight percent, preferably 0.2 to 3 weight percent, and more preferably 0.3 to 1 weight percent of the composition. In the more preferred form, the amount of **vitamin A** dosage is about 500,000 IU / gram per unit dose. **Vitamin A** is toxic at high levels, such that no more than 400,000 IU should be cumulatively ingested per day for greater. . .

SUMM . . . amount" means that amount of the pharmaceutical composition that provides a therapeutic benefit in the treatment, prevention, or management of **skin** wrinkles and other **skin** conditions.

DETD

Ingredient	Weight Percent (% w/w)	Amount (mg)	Chemical or Scientific Name (if different)
N-Acetylglucosamine	17.1	140	N-Acetyl D-Glucosamine
Vitamin C (81.2% Ascorbic Acid)	15	123.2	
L-Lysine (80%)	12.2	100	L-Lysine hydrochloride
L-Proline	11	90	
D-Glucosamine Sulfate (75%)	6.5	53.3	
Chondroitin Sulfate (80%)	6.1	50	
Vitamin E Succinate	4.3	39.7	D-.alpha. tocopheryl acid succinate
Zinc monomethionine (20%)	3.7	30	Zinc DL-methionine
N-Acetyl Cysteine	3.7	30	
Manganese Ascorbate	2.8	23.1	

(13% Mn)
Vitamin B.sub.3
2.4 20 Niacinamide
Niacinamide
Quercetin Powder
2.4 20 Quercetin dihydrate
Grape Seed Extract
0.9 7.5 Proanthocyanidin
Pyridoxal 5 Phosphate-Co B.sub.6 0.6 5 P-5-P monohydrate
Selenoinethionine
(0.5%) 0.5 4 L-selenomethionine
Vitamin A Palmitate
(500,000 IU/GR) 0.5 4
Copper Sebacate (14%) 0.4 2.9
Red beet root powder
6.1 50 Beta vulgaris rubra
Stearic acid 1.5 12
Sorbitol 1.3 11
Acdisol. . .

DETD . . . 73 female subjects to determine the effects on the elasticity, firmness, and presence of fine lines and wrinkles of the **skin**. A seven day conditioning period was used prior to initiation of the study, where subjects were instructed to discontinue use. . .

DETD The texture of the **skin**, fine lines, and wrinkles were assessed by taking Silflo replicas of the periorbital area (crow's feet) at each of the. . . replicas, were illuminated at a precisely defined angle of 350 to create shadows for analysis by shades of gray. The **skin** topography is defined by the: (a) number of wrinkles; (b) total area of wrinkles; (c) total length of wrinkles; (d). . .

DETD . . . is a function of the length of treatment as indicated above. This strongly suggests the treatment has imparted an improved **skin** infrastructure by beneficially affecting the dermis of the **skin**.

DETD The Ballistometer is an instrument designed to evaluate in vivo, in a non-invasive manner, the viscoelastic properties of the **skin**. It analyzes the bounce pattern displayed by a probe that is allowed to impact on the **skin**. The kinetic energy of the probe striking the **skin** is stored by the elastic components of the **skin** and released back to make the probe rebound to a lower height. The height to which the probe will rebound depends upon the amount of stored energy lost in shear viscosity within the **skin** .

DETD The capacity of the **skin** to absorb mechanical energy may thus be measured. Although it is unclear exactly which layer, or layers, of the **skin** are responsible, the mechanical properties of the dermis/epidermis layers are controlled by the density and geometry of the network of. . .

DETD . . . less of the energy of the striking probe was restored, thus, a greater amount of energy was dissipated in the **skin**. This suggests the **skin** became softer and more yielding during the test period.

DETD The Cutometer is a commercially available instrument (Courage & Khazaka, Germany) designed to measure the mechanical properties of the **skin** in a non-invasive manner. It measures the vertical deformation of the **skin**'s surface when pulled by vacuum suction (500 mm Hg) through the small aperture (2 mm) of a probe and the

depth of penetration of the **skin** into the probe optically with an accuracy of 0.01 mm. The probe is attached to a computer, which completely controls probe operation and plots **skin** deformation as a function of time. From this curve, a number of variables can be extrapolated to estimate the elastic, viscoelastic, and purely viscous behavior of the **skin**.

DETD . . . final distension (U.sub.f), measured at 10 seconds; and (d) immediate retraction (U.sub.r). The deformation parameters are extrinsic parameters dependent on **skin** thickness, and a variety of biologically important ratios were calculated: (a) U.sub.r /U.sub.f, a measure of net elasticity of the **skin**; (b) U.sub.r /U.sub.c, the biological elasticity, or measurement of the ability of the **skin** to regain its initial configuration after deformation; and (c) U.sub.v /U.sub.c, the viscoelastic to elastic ratio, where an increase in. . .

DETD . . . distension (U.sub.v) decreased a significant 16 percent ($p<0.04$) after 5 weeks of treatment. This parameter reflects viscoelastic properties of the **skin** and, thus, the behavior of the dermis. After 5 weeks, there were no statistically significant changes in U.sub.c, the immediate. . .

DETD The general appearance of soft, smooth **skin** depends largely on the presence of an adequate amount of water in the stratum corneum. The Corneometer is a commercially available instrument (Courage & Khazaka, Germany) to measure the changes in capacitance of the **skin** resulting from changes in the degree of hydration. It is particularly sensitive to low levels of hydration, and uses measurements of arbitrary units of **skin** hydration (H) to express capacitance.

DETD . . . moisturizing agents and humectants. Thus, the measurements with the Ballistometer and Cutometer indicate changes occurred in deeper layers of the **skin**, rather than the superficial stratum corneum. Table IV shows no significant changes in the hydration of the stratum corneum following. . .

DETD TABLE IV

Corneometer Readings				
	Skin Hydration (H)			
	Mid-Baseline		Final-Baseline	
	Control	Treated	Control	Treated
Average	-5	-7	-8	-4
Standard Deviation	6	7	5	7
p value	p <. . .			

CLM What is claimed is:

1. An orally administered pharmaceutical composition for the prevention and treatment of **skin** conditions in a patient comprising the following components: a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**; a primary antioxidant component in an amount sufficient to substantially inhibit the activity of collagenase and elastase; at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**; at least one transition metal component in an amount effective to bind collagen and elastic fibers and thicken **skin**; and a catechin-based component present in an amount sufficient to inhibit the presence of anti-collagen enzyme in the **skin**.

10. The pharmaceutical composition of claim 7, further comprising a **vitamin E** source, a cysteine source, a **vitamin B.sub.3** source, quercetin dihydrate,

pyridoxal 5 phosphate-Co B.sub.6, a methionine source, and a **vitamin A** source.

11. The pharmaceutical composition of claim 10, wherein the **vitamin E** is D-alpha tocopheryl acid succinate present in about 1 to 15 weight percent, the **vitamin B. sub.3** is niacinamide present in about 0.5 to 15 weight percent, the **vitamin A** is **vitamin A palmitate** present in about 0.1 to 5 weight percent, the cysteine is N-acetyl cysteine present in about 1 to 10 weight. . .

12. An orally administered pharmaceutical composition for the prevention and treatment of **skin** conditions in a patient comprising: an N-acetylglucosamine compound, or a pharmaceutically acceptable salt or ester thereof, present in about 5. . . metal compound is zinc, manganese, or copper, or mixtures thereof, present in about 0.5 to 15 weight percent to thicken **skin**.

13. A method for the prevention or treatment of **skin** conditions, wherein the **skin** has a thickness of dermis and collagen, which comprises orally administering to a patient a pharmaceutical composition comprising: a sugar compound that is converted to a glycosaminoglycan in the patient in an amount sufficient to thicken the **skin**; a primary antioxidant component in an amount sufficient to substantially inhibit the activity of collagenase and elastase; at least one amino acid component in an amount sufficient to assist in the thickening of the **skin**; and at least one transition metal component in an amount effective to bind collagen and elastic fibers and thicken **skin**, said composition administered in an amount therapeutically effective to modify the thickness of the **skin** to prevent or treat at least one **skin** condition.

14. The method of claim 13, wherein the **skin** condition prevented or treated is at least one of wrinkles or the appearance thereof, fine lines or the appearance thereof, thinning, reduced **skin** elasticity, reduced **skin** moisture, spider veins, senile purpura, sun damaged **skin**, aging **skin** or rough **skin**.

. . . conjunction with concurrent or subsequent treatment by at least one additional pharmaceutical composition for the prevention or treatment of a **skin** condition.

. . . comprising providing a catechin-based component present in an amount sufficient to inhibit the presence of an anti-collagen enzyme in the **skin**.

L7 ANSWER 16 OF 18 USPATFULL
AN 97:68148 USPATFULL
TI Personal product compositions comprising heteroatom containing alkyl aldonamide compounds
IN Vermeer, Robert, Nutley, NJ, United States
PA Lever Brothers Company, Division of Conopco, Inc., New York, NY, United States (U.S. corporation)
PI US 5653970 19970805 <--
AI US 1994-352008 19941208 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Gardner, Sallie M.
LREP Koatz, Ronald A.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1

DRWN No Drawings
LN.CNT 6060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5653970 19970805 <--
AB The invention relates to personal product compositions containing heteroatom containing alkyl aldonamide compounds and **skin** conditioning agent. Unexpectedly, applicants have found that when these heteroatom containing alkyl aldonamides are used, benefits such as enhanced stability. . .
SUMM . . . For this reason, a special importance is attached in the cosmetic area to personal products particularly, bath preparations, cleansing preparations, **skin** care preparations, shaving preparations and deodorant or antiperspirant preparations.
SUMM The primary function of a personal product composition is to cleanse the **skin** gently without irritation or excessive defatting or overdrying the **skin**. In addition, successful personal product compositions should not leave the **skin** tight or taut after frequent routine use. After accomplishing the cleansing action, the personal product composition should leave the **skin** feeling soft, smooth, silky and moisturized while simultaneously providing a rich copious foam or lather. This has become a difficult. . . in making a totally satisfactory product. For one thing, it is known that certain mild surfactant systems when formulated for **skin** cleansing, often exhibit poor foam or low lather performance. On the other side, the use of high sudsing surfactants with lather boosters can yield acceptable lather volume, unfortunately however, such surfactant systems are usually harsh to the **skin**. It will be appreciated that these two factors make the formulation process, a delicate balancing act.
SUMM . . . a personal product composition of the invention, surprisingly provides improved foam, viscosity, clarity and conditioning characteristics while simultaneously making the **skin** feeling soft, smooth, silky and moisturized. These findings are quite unexpected and have not been recognized or appreciated in the. . .
SUMM . . . roll-on, stick, tablet, powdered and bar form. Included among the personal product compositions are bubble bathes, shower gels, body shampoos, **skin** cleansers or lotions, liquid soaps, toilet bars, syndet bars, sunscreens, shaving creams, deodorants or antiperspirants and the like.
SUMM . . . good shelf life and should not become turbid or produce sedimentation upon standing. Ideal personal product compositions should cleanse the **skin** gently and should not overdry the **skin**. Surprising the personal product compositions of the present invention that comprise a heteroatom containing alkyl aldonamide compound produce clear, stable,. . .
SUMM . . . alkyl carboxybetaines) and mixtures thereof, could result in a clear thickened personal product composition that foams copiously and leaves the **skin** feeling soft, smooth, silky and moisturized.
SUMM U.S. Pat. No. 4,973,473 to Schneider, et al. teaches **skin** treatment compositions in which the primary moisturizing agent may be a gluconamide compound. Methyloxypropyl gluconamide is the only example of. . .
SUMM These compounds are said to be useful as emollients which are substantive to **skin** or hair and are further taught in U.S. Pat. Nos. 3,990,991 to Gerstein, 4,534,964 to Herstein et al. and 4,529,588. . .
SUMM . . . the heteroatom containing alkyl aldonamide compounds of the invention in compositions with for example, certain essential ingredients such as cosurfactants, **skin** conditioning agents, **skin** feel mildness agents, suspending agents, hydroxy acids, auxiliary thickening agents and auxiliary agents (see claim 4). There is also clearly. . .

SUMM . . . object of the present invention to provide mild personal product compositions that efficiently remove surface grease and dirt from the **skin**.

SUMM It is still another object of the present invention to provide new and improved personal product compositions that leave the **skin** feeling fragrant, soft, smooth, silky and moisturized.

SUMM It is a final object of the present invention to provide an improved method of cleansing and conditioning the **skin**. These and other objects will become readily apparent from the detailed description which follows.

DETD . . . sought. Such ingredients are well known to those skilled in the art and include, but are not limited to cosurfactants, **skin** conditioning agents, **skin** feel mildness agents, suspending agents, hydroxy acids, auxiliary thickening agents, water and other optional ingredients (auxilary agents).

DETD Cationic surfactants have been taught in the art as conditioning agents for the **skin**. Suitable cationic surfactants are broadly exemplified as those of the general formula:

DETD **Skin** Conditioning Agents (Moisturizers/Emollients)

DETD Various materials have been taught in the art for use as agents that condition the **skin**. In general, such conditioning agents are designed to make the **skin** feel soft, smooth, silky and moisturized.

DETD . . . term emollient, and is meant to describe a material which imparts a soft, smooth, silky and moisturized feeling to the **skin** surface.

DETD One way of moisturizing is to reduce the rate of water loss from the stratum corneum (**skin** surface) by depositing an occlusive material (emollient or emulsifier) on the **skin** surface which prevents water evaporation. Mother technique is to add hygroscopic nonocclusive substances (humectants), which will retain water to the stratum corneum, making water available to the **skin** surface thereby producing the desired cosmetic effect. Nonocclusive moisturizers also function by improving the lubricity of the **skin**. Both occlusive and nonocclusive moisterizers as well as mixtures thereof are operative in the present invention. Examples of occulusive moisturizers.. . . include polyols, fatty acids, certain alkanolamides, pyrrolidone carboxylic acid and their derivatives. It is to be understood that any such **skin** conditioning agent or mixtures thereof can be employed herein, depending on the formulations desires.

DETD . . . decyl neopentanoate, myristyl propionate, decyl oleate, isopropyl myristate, lauryl myristate, myristyl myristate, myreth-3-myristate, palmityl myristate, stearyl myristate, isopropyl palmirate, octyl **palmitate**, 2-ethylhexyl palmirate, lauryl **palmitate**, myristyl palmirate, palmityl **palmitate**, stearyl palmirate, butyl stearate, myristyl stearate, palmityl stearate, isocetyl stearate, isostearyl isostearate, oleyl myristate, oleyl stearate, oleyl oleate, methyl cocoate,. . . butanediol, PPG-8-C.sub.12 -C.sub.20 alkyl ester, Peg-45 palm kernel glyceride, neopentylglycol dicaprylate/dicaprate, C.sub.12 -C.sub.15 alcohol benzoate, diisoarachidyl dilinoleate, dioctyl maleate, ascorbyl **palmitate**, diisopropyl adipate, diisohexyl adipate, dihexadecyl adipate, diisopropyl sebacate, dioctyl succinate, didecyl succinate, jojoba esters and the like.

DETD . . . potassium, ammonium and alkanol ammonium salts of pyrrolidone carboxylic acid, ethyl pyrrolidone carboxylic acid and the like. Typical levels of **skin** conditioning agent are from about 1% to about 40%, preferably from about 2% to about 30%, even more preferably from. . .

DETD **Skin** Feel Mildness Agents

DETD The **skin** feel mildness agents useful in the present invention

include, but are not limited to the cationic, anionic, amphoteric and nonionic polymers used in the cosmetic field. Reduced **skin** irritation benefits of cationic and nonionic polymers are described in Polymer JR for **Skin** Care Bulletin, by Union Carbide in (1977). The cationic polymers also provide a desirable soft, smooth and silky feeling to the **skin**. While wishing not to be bound to theory, it is believed that cationic polymers chemically interact with anionic surfactants to form complexes which may enhance overall mildness to **skin** characteristics. Also, there is a reason to believe that positively charged cationic polymers can bind with negatively charged sites on the **skin** to provide a softer **skin** feel after use. The cationic polymers are most preferred because they provide the best **skin** feel benefits.

DETD . . . in the present invention is discribed in U.S. Patent No. 4,438,095 which is incorporated herein by reference. Typical levels of **skin** conditioning agent are from about 0% to about 5%, preferably from about 0% to about 4%, even more preferably from. . .

DETD Hydroxy acids have been taught in the art for use as agents that exfoliate dead **skin** cells leaving **skin** smoother and tighter with a more youthful appearance. In addition, hydroxy acid treatments help reduce liver and sun spots as. . .

DETD . . . and vegetables or by fermentation of corn or sugar substrates) and the like are useful as well. Typical levels of **skin** conditioning agent are from about 0% to about 10%, preferably from about 0% to about 8%, even more preferably from. . .

DETD Various materials have been taught in the art as agents that are useful in suspending certain performance ingredients such as **skin** feel mildness agents, silicone fluids, and the like, uniformly, thereby assisting in the delivery of the desirable performance attributes associated. . .

DETD Examples of sunscreens or UV absorbers useful in the present invention which protect the **skin** and certain sensitive ingredients from harmful sunlight include dipropyleneglycol salicylate, octyl salicylate, 2-ethylhexyl p-dimethylaminobenzoate (octyldimethyl-PABA), polyoxyethylene p-dimethylaminobenzoate (PEG-25 PABA), Tri-PABA-panthenol,. . .

DETD Examples of vitamins useful in the present invention which provide the hair with valuble nutrition include **vitamin A** (as retinyl acetate, propionate or **palmitate**) provitamin A (based on carrot extract, as .beta.-carotene), vitamin B.sub.1 (as thiamine mononitrate), vitamin B.sub.2 (as riboflavin), **vitamin B.sub.3** (as niacinamide), vitamin B.sub.5 (as pantothenic acid), provitamin B.sub.5 (as panthenol), vitamin B.sub.6 (as pyridoxine hydrochloride, dioctenoate, dilaurate, dipalmitate or tripalmitate), vitamin B.sub.12 (as cyanocobalamin), vitamin B.sub.15 (as pangamic acid), **vitamin C** (as ascorbic acid), vitamin D.sub.2 (as ergocalciferol), vitamin D.sub.3 (as cholecalciferol), **vitamin E** (as dl-.alpha.-tocopherol acetate, linoleate or nicotinate,), vitamin F (as glyceryl linoleate and glyceryl linolenate), vitamin K.sub.1 (as phytonadione), vitamin K.sub.3. . . bioflavoniod and mixtures thereof. Preferred vitamins are provitamin A, vitamin B.sub.1, vitamin B.sub.2, provitamin B.sub.5, vitamin B.sub.6, vitamin B.sub.12 and **vitamin E**. Typical levels of vitamin are from about 0% to about 7% by weight of the composition.

DETD Examples of amino acids useful in the present invention which provide the **skin** with valuble nutrition include alanine, .beta.-alanine, N-methylalanine, N-phenylalanine, .alpha.-aminoisobutyric acid, .alpha.-aminobutyric acid, .alpha.-aminocaproic acid, .epsilon.-aminocaproic acid, glycine, N-ethylglycine, N-propylglycine, N-butylglycine,. . . (keratin polypeptides), silk amino acids, allantoin acetyl methionine, allantoin, deoxyribonucleic

acid, protamine/nucleic acid complex, nucleic acid, collagen amino acids, retinyl **palmitate** polypeptide, proline, polyglucan and mixtures thereof. Preferred amino acids are glycine, methionine, sarcosine, keratin amino acids and silk amino acids.. . .

DETD Examples of proteins useful in the present invention which provide the **skin** with valuble nutrition include hydrolyzed casein, hydrolyzed collagen (hydrolyzed animal protein), myristoyl hydrolyzed animal protein, hydrolyzed corn protein, hydrolyzed glycosaminoglycans,. . .

DETD . . . present invention which prevent the oxidation of certain ingredients by air and prevent the development of unpleasant, rancid odors include **vitamin E** (tocopherol), lecithin, wheat germ oil, sodium sulfite, sodium bisulfite, uric acid, propyl gallate, butylated hydroxyanisole (BHA), toluhydroquinone (THQ) sold as. . .

DETD . . . adjusted to a pH of about less than 7 to provide a composition that is non-irritating and non-damaging to the **skin** of the consumer. The amount of buffering agent used will be that which is sufficient to provide the desired buffered. . .

DETD Examples of heeling agents which function to stimulate the growth of healthy **skin** tissue include allantion, aluminum dihydroxy allantoinate, urea, uric acid, aloe vera gel, methyl manuronate, uronic acids, sucrose octaacetate, menthol, hydrolyzed. . .

DETD (c) from about 1% to about 40% by weight of the composition is a **skin** conditioning agent;

DETD (d) from about 0% to about 5% by weight of the composition is a **skin** feel mildness agent;

DETD (c) from about 2% to about 30% by weight of the composition is a **skin** conditioning agent;

DETD (d) from about 0% to about 4% by weight of the composition is a **skin** feel mildness agent;

DETD (c) from about 3% to about 25% by weight of the composition is a **skin** conditioning agent;

DETD (d) from about 0% to about 3% by weight of the composition is a **skin** feel mildness agent;

DETD (c) from about 3.1% to about 25% by weight of the composition is a **skin** conditioning agent;

DETD (d) from about 0% to about 3% by weight of the composition is a **skin** feel mildness agent;

DETD . . . in a variety of types and forms. A classification according to product type would consist of bath products, cleansing products, **skin** care products, shaving products and deodorant/antiperspirant products.

DETD Examples of **skin** care products include, but are not limited to hand/body/facial moisturizers, hand/body/facial creams, massage creams, hand/body/facial lotions, sunscreen products, tanning products,. . .

DETD . . . the heteroatom containing alkyl aldonamide compounds of the invention are useful as foam stabilizing agents, thickening agents, solubilizing agents and **skin** conditioning agents. In addition, it has been found that the heteroatom containing alkyl aldonamide compounds of the invention are also. . .

DETD The present compositions are used in a conventional manner for cleaning and/or conditioning the **skin**. From about 0.1 g to about 15 g of a composition is applied to the **skin** that may or may not be thoroughly wetted with water. The composition is worked unto the **skin** from about 30 seconds to about five minutes and then rinsed off or left on.

DETD The zein solubilization assay was developed to determine the biological effects of surfactants on the **skin**. The protein is normally in soluble in water, but can be brought into solution by interaction with surfactants. The extent. . . Z. Poly., 233, 848, 1969). The greater the zein solubilization, the greater the irritation potential of that

surfactant on the **skin**.

DETD In order to demonstrate the improved ability of heteroatom containing alkyl aldonamide to provide mildness benefits to the **skin**, mixtures of C.sub.8 /C.sub.10 oxypropyl D-gluconamide (C.sub.8 /C.sub.10 OPG) and sodium lauryl sulfate (SLS) by weight were tested and compared. . .

DETD . . . so the heteratom containing alkyl aldonamide compounds not anly enhance viscosity and stabilize foam, but are also mild to the **skin**.

DETD High Foaming **Skin** Conditioning Bubble Bath

DETD High Foaming **Skin** Conditioning Bubble Bath Concentrate with Protein

DETD . . . Laurate

13. PEG-30 Glyceryl -- -- -- -- -- -- 4.0
Cocoate

14. PEG-200 -- -- -- -- -- -- 4.0
Glyceryl
Palmitate

15. Glyceryl Laurate 1.0 -- -- -- -- -- --

16. C8/C10 1.0 -- -- -- 1.0 -- 1.0
Oxypropyl D-
Gluconamide

17.. . . 3.0 --

32. Hena Extract -- -- -- -- -- 0.5 --

33. Tocopherol -- 0.5 -- -- -- -- 1.0
Acetate
(**Vitamin E**)

34. Panthenol 0.5 -- -- -- -- -- --
(Vitamin B5)

35. Ethylene Glycol -- -- 0.6 -- -- -- --
Monostearate

36.. . .

DETD . . . -- 0.6 -- --

31. Panthenol -- -- -- 2.0 -- -- --
(Vitamin B5)

32. Tocopheryl -- -- -- 2.0 -- -- --
Acetate/Linoleate
(**Vitamin E**)

33. Butylated 0.01 0.01 -- -- -- 0.1 --
Hydroxytoluene

34. Carboxymethyl -- -- -- 1.5 -- -- --
Cellulose

35. Hydroxyethyl -- -- --. . .

DETD . . . 2.0 --

27. Kelp Extract -- -- -- -- -- -- 2.0

28. Tocopheryl Ace- -- -- -- -- -- -- 0.5
tate (**Vitamin E**)

29. Sodium 5.0 5.2 -- -- 5.0 -- --
Isethionate

30. Sodium Chloride 0.5 0.5 0.5 0.5 0.4 -- --

31. Titanium Dioxide
0.5. . .
DETD A Mild Moisturizing Syndet Bar Composition with **Vitamin E** and Bath Oil
DETD . . . -- --
Protein
54. TEA-Coco
-- -- -- -- -- -- 18.0
Hydrolyzed Animal Protein
55. Tocopheryl Ace-
-- -- -- -- -- -- 0.3
tate (**Vitamin E**)
56. Sodium -- 0.2 -- -- 0.3 -- --
Dehydroacetate
57. Sodium Pyrroli-
-- -- -- -- -- 4.0 --
done Carboxylic Acid
58. Disodium. . .
DETD An Astringent Facial Cleansing Composition with Protein, **Vitamin E** and Aloe
DETD . . . Acetylated Lanolin
-- -- 0.2 -- -- -- --
Alcohol
31. C.sub.12 -C.sub.15 Alcohol
-- -- 0.4 -- 4.0 -- --
Benzoate
32. Octyl **Palmitate**
-- -- -- -- -- 2.5 --
33. Methyl Glucose -- -- 0.8 -- -- --
Sesquistearate
34. Diisoarachidyl
-- -- 1.0 -- -- -- --
Dilinoleate
35. Dioctyl Maleate
-- -- -- -- 5.0 -- --
36. Ascorbyl **Palmitate**
-- -- -- 0.1 -- -- --
37. Stearic Acid (xxx)
-- -- 0.5 -- 1.0 1.0 --
38. Isostearic Acid
-- -- -- -- -- 1.7 --
39. Tocopheryl Ace-
-- -- -- 0.2 -- 0.1 1.0
tate (**Vitamin E**)
40. Panthenol
-- -- -- -- -- -- 1.0
(Provitamin B5)
41. Retinyl **Palmitate**
-- -- 3.0 -- -- -- --
Polypeptide
42. Lecithin
-- -- 10.0 -- -- -- --
43. Proline -- -- -- --. . .
DETD A Moisturizing Lotion Composition with Antioxidants for Aging **Skin**
DETD A Moisturizing Cream Composition with Alpha Hydroxy Acids and **Vitamin E**
DETD . . . -- --
(2%)
46. Carbomer 940
-- -- -- -- -- 10.0 5.0

(2%)
47. Tocopheryl Ace-
-- -- -- 0.1 0.2 -- 0.2
tate (**Vitamin E**)
48. Ascorbic Acid
-- -- -- -- 0.3 -- --
(**Vitamin C**)
49. Ascorbyl **Palmitate**
-- -- -- -- -- -- 0.2
50. Retinyl **Palmitate**
-- -- -- -- -- -- 0.3
(**Vitamin A**)
51. Bioflavoniod
-- -- -- -- -- -- 0.4
52. Ivy Extract
-- -- -- -- -- -- 0.9
53. Dimethicone
-- --. . .
DETD A Sunscreen Cream Composition with **Vitamin E**
DETD A Sunscreen Cream Composition with **Vitamin E**
DETD . . . --
35. Animal -- -- -- 0.5 0.1 -- --
Collagen
(Soluble)
36. Tocopheryl -- -- -- -- 0.1 -- --
Acetate
(**Vitamin E**)
37. Acetamide -- -- -- 1.5 -- -- --
MEA
38. Lactamide -- -- -- 1.5 -- -- --
MEA
39. Allantoin --. . .
DETD A Nonalcoholic Aftershave Lotion Composition with **Vitamin E**
DETD An Aftershave **Skin** Conditioning Composition
CLM What is claimed:
. . . ammonium chloride, sodium sulfate, potassium sulfate, magnesium sulfate, sodium isethionate, sodium thiosulfate and mixtures thereof; (d) about 1% to 40% **skin** conditioning agent; and (e) water.

L7 ANSWER 17 OF 18 USPATFULL
AN 97:53932 USPATFULL
TI Hair care compositions comprising heteroatom containing alkyl aldonamide compounds
IN Vermeer, Robert, Nutley, NJ, United States
PA Lever Brothers Company, Division of Conopco, Inc., New York, NY, United States (U.S. corporation)
PI US 5641480 19970624 <--
AI US 1994-352309 19941208 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Gardner, Salle M.
LREP Koatz, Ronald A.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5444
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5641480 19970624 <--
SUMM . . . to cleanse the hair and scalp from soil without stinging or irritating the eyes and scalp. Hair soil includes natural **skin**

secretions (such as sebum), **skin** debris, dirt from the environment and residue from hair-grooming products applied by the consumer. After accomplishing the cleansing action, the. . .

SUMM U.S. Pat. No. 4,973,473 to Schneider, et al. teaches **skin** treatment compositions in which the primary moisturizing agent may be a gluconamide compound. Methyloxypropyl gluconamide is the only example of. . .

SUMM These compounds are said to be useful as emollients which are substantive to **skin** or hair and are further taught in U.S. Pat. Nos. 3,990,991 to Gerstein, 4,534,964 to Herstein et al. and 4,529,588. . .

SUMM . . . still another object of the present invention to provide mild hair care compositions that efficiently remove surface grease, dirt and **skin** debris from the hair shaft and scalp.

SUMM . . . the hair. Examples of such conditioning agents include, lanolin and its derivatives, long chain esters such as isopropyl myristate, butyl **palmitate**, stearyl stearate, carylic/capric triglycerides, polyols such as glycerol (glycerin), propylene glycol and the like, oils, amine oxides, fatty alcohols, carbohydrates,. . .

SUMM . . . cetyl lactate, stearyl lactate, decyl neopentanoate, decyl oleate, isopropyl myristate, lauryl myristate, myristyl myristate, myreth-3-myristate, palmityl myristate, stearyl myristate, isopropyl **palmitate**, octyl **palmitate**, 2-ethylhexyl palmirate, lauryl palmirate, myristyl **palmitate**, palmityl palmirate, stearyl **palmitate**, butyl stearate, myristyl stearate, palmityl stearate, isocetyl stearate, isostearyl isostearate, myristyl alcohol, cetyl alcohol, isocetyl alcohol, stearyl alcohol, oleyl alcohol,. . .

SUMM Examples of vitamins useful in the present invention which provide the hair with valuable nutrition include **vitamin A** (as retinyl acetate, propionate or **palmitate**) provitamin A (based on earrot extract, as .beta.-carotene), vitamin B.sub.1 (as thiamine mononitrate), vitamin B.sub.2 (as ribofiavin), **vitamin B.sub.3** (as niacinamide, vitamin B.sub.5 (as pantothenic acid), provitamin B.sub.5 (as panthenol), vitamin B.sub.6 (as pyridoxine hydrochloride, dioctenoate, dilaurate, dipalmitate or tripalmitate), vitamin B.sub.12 (as cyanocobalamin), vitamin B.sub.15 (as pangamic acid), **vitamin C** (as aseorbie add), vitamin D.sub.2 (as ergocalciferol), vitamin D.sub.3 (as cholecalciferol), **vitamin E** (as dl-.alpha.-tocopherol acetate, linoleate or nicotinate,), vitamin F (as glyceryl linoleate and glyceryl linolenate), vitamin K.sub.1 (as phytonadione), vitamin K.sub.3. . . sterol and mixtures thereof. Preferred vitamins are provitamin A, vitamin B.sub.1, vitamin B.sub.2, provitamin B.sub.5, vitamin B.sub.6, vitamin B.sub.12 and **vitamin E**. Typical levels of vitamin are from about 0% to about 7% by weight of the composition.

SUMM . . . present invention which prevent the oxidation of certain ingredients by air and prevent the development of unpleasant, rancid odors include **vitamin E** (tocopherol), lecithin, wheat germ oil, sodium sulfite, sodium bisulfite, uric acid, propyl gallate, butylated hydroxyanisole (BHA), toluhydroquinone (THQ) sold as. . .

SUMM . . . to a pH of about less than 7 to provide a composition that is non-irritating and non-damaging to the hair, **skin** and eyes of the consumer. The mount of buffering agent used will be that which is sufficient to provide the. . .

DETD The zein solubilization assay was developed to determine the biological effects of surfactants on the **skin**. The protein is normally in soluble in water, but can be brought into solution by interaction with surfactants. The extent. . . Z. Poly., 233, 848, 1969). The greater the zein solubilization, the greater the irritation potential of that surfactant on the **skin**.

DETD In order to demonstrate the improved ability of heteroatom containing alkyl aldonamtde to provide mildness benefits to the **skin** (scalp), mixtures of C.sub.8 /C.sub.10 oxypropyl D-gluconamide (C.sub.8 /C.sub.10 OPG) and sodium lauryl sulfate (SLS) by weight were tested and. . .

DETD . . . Protein
-- -- -- -- -- -- 1.0
33. Wheat Germ Oil -- -- -- -- -- 0.1
--
34. Tocopherol Acetate (**Vitamin E**)
-- -- -- -- -- 0.1
--
35. Panthenol (Provitamin B5)
-- -- -- -- -- 0.5
--
36. Balsam -- --. . .

L7 ANSWER 18 OF 18 USPATFULL
AN 97:51727 USPATFULL
TI Method for determining diet program effectiveness
IN Chait, Allen, Seattle, WA, United States
Hatton, Dan, Portland, OR, United States
Haynes, R. Brian, Dundas, Canada
Khoo, Chor San Heng, Mt. Laurel, NJ, United States
Kris-Etherton, Penny, State College, PA, United States
Macnair, R. David C., King of Prussia, PA, United States
McCarron, David, Portland, OR, United States
Metz, Jill, Portland, OR, United States
Oparil, Suzanne, Birmingham, AL, United States
Pi-Sunyer, Xavier, New York, NY, United States
Resnick, Larry, West Bloomfield, MI, United States
Stern, Judith S., Lafayette, CA, United States
Ziegler, Paula J., Cherry Hill, NJ, United States
PA Campbell Soup Company, Camden, NJ, United States (U.S. corporation)
PI US 5639471 19970617 <--
AI US 1995-469516 19950606 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Shelborne, Kathryne E.
LREP Baker & Botts, L.L.P.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 3163
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5639471 19970617 <--
SUMM The NCI also suggests that diets rich in foods containing **Vitamin C** and **Vitamin A** from fruits and vegetables may also reduce the risk of cancer. Epidemiologic studies have shown that diets high in **Vitamin A** and **Vitamin C** are associated with lower risks of some kinds of cancers. Therefore, the NCI recommends consumption of a variety of fruits and vegetables, including fruit and vegetable juices that are high in **Vitamin A** and **Vitamin C**. Especially beneficial are cruciferous vegetables which are good sources of fiber, as well as vitamins and minerals.
DRWD . . . major sources of dietary fat rather than by eliminating whole categories of foods. For example, by substituting fish, poultry without **skin**, lean meats and low- or non-fat dairy products for high-fat foods, a patient may lower total fat and SFA intake. . .
DRWD TABLE I

Nutrient	Daily Desired Level of Fortification Breakfast Meal (35%)	Lunch Meal (30%)	Dinner Meal (35%)
VITAMIN A, (IU)	1750	1500	1750
VITAMIN D, (IU)	140	120	140
VITAMIN E, (IU)	10.5	9	10.5
VITAMIN C, (mg)	35	30	35
VITAMIN B.sub.1, (mg)	0.53	0.45	0.53
VITAMIN B.sub.2, (mg)	0.6	0.51	0.6
VITAMIN B.sub.3, (mg)	7	6	7
VITAMIN B.sub.6, (mg)	0.7	0.6	0.7
VITAMIN B.sub.12, (mg)	2.1	1.8	2.1
BIOTIN, (mcg)	105	90	105
FOLIC ACID, (mg)			

. . .

DRWD TABLE III

U.S. Recommended Dietary AHowance (USRDA)

NUTRIENT	USRDA
VITAMIN A	5000 IU
VITAMIN B.sub.1	1.5 mg
VITAMIN B.sub.2	1.7 mg
VITAMIN B.sub.3	20 mg NE.sup.1
VITAMIN B.sub.6	2 mg
VITAMIN B.sub.12	6 mcg
VITAMIN C	60 mg
VITAMIN D	400 IU
VITAMIN E	30 IU
VITAMIN K	NONE ESTABLISHED
BIOTIN	300 mcg
CALCUIM	1000 mg
COPPER	2 mg
FOLIC ACID	400 mcg
IODINE	150 mcg
IRON	18 mg
MAGNESIUM	400 mg
MANGANESE. . .	

DRWD TABLE IV

DFEA Compositions

NUTRIENT	CONCENTRATION RANGE
VITAMIN A	1125-9900 IU
VITAMIN B.sub.1	0.41-2.07 mg
VITAMIN B.sub.2	0.23-2.24 mg

VITAMIN B.sub.3
6.3-25.3 mg NE
VITAMIN B.sub.6
0.54-2.75 mg
VITAMIN B.sub.12
1.08-8.58 mcg
VITAMIN C 31.5-330 mg
VITAMIN D 36-682 IU
VITAMIN E 9.45-49.5 IU
VITAMIN K 0-110 mcg
BIOTIN 94.5-412.5 mcg
CALCUIM 108-1333.2 mg
COPPER 0.95-3.63 mg
FOLIC ACID 126-660 mcg
IODINE 47.25-187.75 mcg
IRON 5.67-20.79 mg
MAGNESIUM 72-339.9 mg
MANGANESE. . .
DETD

TABLE VIII

Vitamin and Mineral Mixture (Frozen Foods)

NUTRIENT	CONCENTRATION	FORM
VITAMIN A	9000 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	1.88 mg	Thiamine Mononitrate
VITAMIN B.sub.2	2.04 mg	Riboflavin
VITAMIN B.sub.3	23 mg NE	Niacinamide
VITAMIN B.sub.6	2.5 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	7.8 mcg	Vitamin B.sub.12
VITAMIN C	300 mg	Ascorbic Acid
VITAMIN D	620 IU	Vitamin D.sub.3
VITAMIN E	45 IU	**Vitamin E** Acetate
VITAMIN K	100 mcg	Vitamin K.sub.1
BIOTIN	375 mcg	Biotin
CALCUIM	1212 mg	Calcium Citrate/Dicalcium Phosphate
COPPER	3.3 mg	Copper Gluconate
FOLIC ACID	600. . .	

DETD . . . humidity, e.g. in a range of about 35 to 75% RH, to produce a homogenous vitamin mix: 36 mg of **Vitamin A Palmitate** (250 micron spray dried); 300 mg of Ascorbic Acid; 6.2 mg of Vitamin D.sub.3 -100 S.D.; 90 mg of **Vitamin E** acetate 50% (CWS/F); 10 mg of Vitamin K.sub.1, 1% (spray dried); 1.88 mg of Thiamine Mononitrate; 2.04 mg of Riboflavin;. . .

DETD

TABLE IX

Vitamin and Mineral Mixture (Cereals)

NUTRIENT	CONCENTRATION	FORM
VITAMIN A	2500 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	0.59 mg	Thiamine Mononitrate

VITAMIN B.sub.2
0.32 mg Riboflavin
VITAMIN B.sub.3
7.7 mg NE Niacinamide
VITAMIN B.sub.6
0.84 mg Pyridoxine Hydrochloride
VITAMIN B.sub.12
2.4 mcg Vitamin B.sub.12
VITAMIN C 140 mg Ascorbic Acid/Sodium Ascorbate
VITAMIN D 80 IU Vitamin D.sub.3
VITAMIN E 15.75 IU **Vitamin E** Acetate
BIOTIN 141.75 mcg Biotin
CALCUIM 123.6 mg Calcium Carbonate
COPPER 1.16 mg Copper Gluconate
FOLIC ACID 210 mcg Folic Acid
IODINE 60.38 mcg Potassium. . .
DETD TABLE X

Vitamin and Mineml Mixture (Soups and Other Retorted Meals)

NUTRIENT	CONCENTRANON	FORM
VITAMIN A	9000 IU	**Vitamin A Palmitate**
VITAMIN B.sub.1	2.63 mg	Thiamine Mononitrate
VITAMIN B.sub.2	2.04 mg	Riboflavin
VITAMIN B.sub.3	23 mg NE	Niacinamide
VITAMIN B.sub.6	2.5 mg	Pyridoxine Hydrochloride
VITAMIN B.sub.12	7.8 mcg	Vitamin B.sub.12
VITAMIN C	300 mg	Ascorbic Acid
VITAMIN D	620 IU	Vitamin D.sub.3
VITAMIN E	45 IU	**Vitamin E** Acetate
VITAMIN K	100 mcg	Vitamin K.sub.1
BIOTIN	375 mcg	Biotin
CALCUIM	1212 mg	Calcium Citrate/Dicalcium Phosphate
COPPER	3.3 mg	Copper Gluconate
FOLIC ACID	600. . .	

DETD TABLE XI

Garlic Roll

Nutrient	Fortification Level
VITAMIN A, (IU)	2250
VITAMIN D, (IU)	155
VITAMIN E, (IU)	11.25
VITAMIN C, (mg)	75
VITAMIN B.sub.1, (mg)	0.47
VITAMIN B.sub.2, (mg)	

0.51
VITAMIN B.sub.3, (mg)
5.75
VITAMIN B.sub.6, (mg)
0.63
VITAMIN B.sub.12, (mg)
1.95
BIOTIN, (mcg) 93.75
FOLIC ACID, (mg) 150
PANTOTHENIC ACID, (mg)
3.13
VITAMIN K, (mcg) 25
CALCIUM, (mg). . .
DETD TABLE XII

Raisin Bran Cereal

Nutrient	Fortification Level
VITAMIN A, (IU)	2500
VITAMIN D, (IU)	80
VITAMIN E, (IU)	15.75
VITAMIN C, (mg)	140
VITAMIN B.sub.1, (mg)	0.59
VITAMIN B.sub.2, (mg)	0.32
VITAMIN B.sub.3, (mg)	7.7
VITAMIN B.sub.6, (mg)	0.84
VITAMIN B.sub.12, (mg)	2.4
BIOTIN, (mcg)	141.75
FOLIC ACID, (mg)	210
PANTOTHENIC ACID, (mg)	4.5
CALCIUM, (mg)	123.6
COPPER, (mg)	1.16
IRON. . .	

DETD TABLE XIII

Apple Crisp

Nutrient	Fortification Level
VITAMIN A, (IU)	1620
VITAMIN D, (IU)	111.6
VITAMIN E, (IU)	8.1
VITAMIN C, (mg)	54
VITAMIN B.sub.1, (mg)	0.34
VITAMIN B.sub.2, (mg)	0.37
VITAMIN B.sub.3, (mg)	4.14
VITAMIN B.sub.6, (mg)	0.45
VITAMIN B.sub.12, (mg)	1.4
BIOTIN, (mcg)	67.5
FOLIC ACID, (mg)	108

PANTOTHENIC ACID, (mg)	2.25
VITAMIN K, (mcg)	18
CALCIUM, (mg). . .	

DETD TABLE XIV

Whipped Potatoes

Nutrient	Fortification Level
VITAMIN A, (IU)	1080
VITAMIN D, (IU)	74.4
VITAMIN E, (IU)	5.4
VITAMIN C, (mg)	36
VITAMIN B.sub.1, (mg)	0.23
VITAMIN B.sub.2, (mg)	0.25
VITAMIN B.sub.3, (mg NE)	2.76
VITAMIN B.sub.6, (mg)	0.3
VITAMIN B.sub.12, (mcg)	0.94
BIOTIN, (mcg)	45
FOLIC ACID, (mcg)	72
PANTOTHENIC ACID, (mg)	1.5
VITAMIN K, (mcg)	12
CALCIUM,. . .	

DETD TABLE XV

Orange Juice Drink

Nutrient	Fortification Level
VITAMIN A, (IU)	1800
VITAMIN D, (IU)	124
VITAMIN E, (IU)	9
VITAMIN C, (mg)	60
VITAMIN B.sub.1, (mg)	0.38
VITAMIN B.sub.2, (mg)	0.41
VITAMIN B.sub.3, (mg NE)	4.6
VITAMIN B.sub.6, (mg)	0.5
VITAMIN B.sub.12, (mcg)	1.56
BIOTIN, (mcg)	75
FOLIC ACID, (mcg)	120
PANTOTHENIC ACID, (mg)	2.5
VITAMIN K, (mcg)	20
CALCIUM,. . .	

DETD TABLE XVI

Vegetable Soup

Nutrient	Fortification Level

VITAMIN A, (IU)	2700
VITAMIN D, (IU)	186
VITAMIN E, (IU)	13.5
VITAMIN C, (mg)	90
VITAMIN B.sub.1, (mg)	0.79
VITAMIN B.sub.2, (mg)	0.61
VITAMIN B.sub.3, (mg NE)	6.9
VITAMIN B.sub.6, (mg)	0.75
VITAMIN B.sub.12, (mcg)	2.34
BIOTIN, (mcg)	112.1
FOLIC ACID, (mcg)	180
PANTOTHENIC ACID, (mg)	3.75
VITAMIN K, (mcg)	30
CALCIUM,. . .	

DETD TABLE XVII

Fruit Sauce

Nutrient	Fortification Level
VITAMIN A, (IU)	450
VITAMIN D, (IU)	31
VITAMIN E, (IU)	2.25
VITAMIN C, (mg)	15
VITAMIN B.sub.1, (mg)	0.09
VITAMIN B.sub.2, (mg)	0.1
VITAMIN B.sub.3, (mg NE)	1.15
VITAMIN B.sub.6, (mg)	0.13
VITAMIN B.sub.12, (mcg)	0.39
BIOTIN, (mcg)	18.75
FOLIC ACID, (mcg)	30
PANTOTHENIC ACID, (mg)	0.63
VITAMIN K, (mcg)	5
CALCIUM,. . .	

DETD TABLE XVIII

Bagel

Nutrient	Fortification Level
VITAMIN A, (IU)	450
VITAMIN D, (IU)	31
VITAMIN E, (IU)	2.25
VITAMIN C, (mg)	15
VITAMIN B.sub.1, (mg)	0.09
VITAMIN B.sub.2, (mg)	0.1
VITAMIN B.sub.3, (mg NE)	1.15

VITAMIN B.sub.6, (mg)
0.13
VITAMIN B.sub.12, (mcg)
0.39
BIOTIN, (mcg) 18.75
FOLIC ACID, (mcg) 30
PANTOTHENIC ACID, (mg)
0.63
CALCIUM, (mg) 60.6
COPPER, (mg). . .
DETD TABLE XIX

Salisbury Steak

Nutrient	Fortification Level
VITAMIN A, (IU)	2700
VITAMIN D, (IU)	186
VITAMIN E, (IU)	13.5
VITAMIN C, (mg)	90
VITAMIN B.sub.1, (mg)	0.54
VITAMIN B.sub.2, (mg)	0.61
VITAMIN B.sub.3, (mg NE)	6.9
VITAMIN B.sub.6, (mg)	0.75
VITAMIN B.sub.12, (mcg)	2.34
BIOTIN, (mcg)	112.1
FOLIC ACID, (mcg)	180
PANTOTHENIC ACID, (mg)	3.75
VITAMIN K, (mcg)	30
CALCIUM,. . .	

DETD TABLE XX

Salisbury Steak Gravy

Nutrient	Fortification Level
VITAMIN A, (IU)	450
VITAMIN D, (IU)	31
VITAMIN E, (IU)	2.25
VITAMIN C, (mg)	15
VITAMIN B.sub.1, (mg)	0.09
VITAMIN B.sub.2, (mg)	0.1
VITAMIN B.sub.3, (mg NE)	1.15
VITAMIN B.sub.6, (mg)	0.13
VITAMIN B.sub.12, (mcg)	0.39
BIOTIN, (mcg)	18.75
FOLIC ACID, (mcg)	30
PANTOTHENIC ACID, (mg)	0.63
VITAMIN K, (mcg)	5
CALCIUM,. . .	

DETD				. . . Fiber (g)
	7	7	7	6
Sugar (g)	18	33	35	23
Protein (g)	21	14	16	13

PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)

Vitamin A	35	35	35	35
Vitamin C	55	55	55	55
Calcium	40	40	40	40
Iron	35	35	35	35
Vitamm D	35	35	35	35
Vitamin E	35	35	35	35
Thiamine	35	35	35	35
Riboflavin	35	35	35	35
Niacin	35	35	35	35
Vitamin B.sub.6	35	35	35. . .	
DETD				. . . 11
Protein (g)	19	26	20	20

PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)

	SPLIT PEA SOUP	CHICKEN NOODLE SOUP	TURKEY SANDWICH	PASTA Meal		
Vitamin A	30	30	30	30		
Vitamin C	50	50	50	50		
Calcium	35	35	35	35		
Iron	30	30	30	30		
Vitamm D	30	30	30	30		
Vitamin E	30	30	30	30		
Thiamine	30	30	30	30		
Riboflavin	30	30	30	30		
Niacin	30	30	30	30		
Vitamin B.sub.6	30	30	30. . .			
DETD				. . . 24	31	27 33

PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)

	GRILLED BBQ CHICKEN	GRILLED MUSTARD CHICKEN	GRILLED HERB ROASTED CHICKEN	CHICKEN	MEATLOAF POT ROAST
Vitamin A	35	35	35	35	35
Vitamin C	55	55	55	55	55
Calcium	40	40	40	40	40
Iron	35	35	35	35	35
Vitamin D	35	35	35	35	35
Vitamin E	35	35	35	35	35
Thiamine	35	35	35	35	35
Riboflavin	35	35	35	35	35

Niacin 35 35 35 35 35
Vitamin. . . 27 28 32 29 25

PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)

	SALISBURY STEAK	SIRLOIN BEEF TIPS	TURKEY TRADITIONAL	TURKEY GLAZED	BEEF STEW
Vitamin A	35	35	35	35	35
Vitamin C	55	55	55	55	55
Calcium	40	40	40	40	40
Iron	35	35	35	35	35
Vitamin D	35	35	35	35	35
Vitamin E	35	35	35	35	35
Thiamine	35	35	35	35	35
Riboflavin	35	35	35	35	35
Niacin	35	35	35	35	35
Vitamin. . .					
DETD				. . .	Fiber (g)
	2	1	3	2	
Sugar (g)	2	1	9	11	
Protein (g)	6	5	11	10	

PERCENTAGE OF U.S. RECOMMENDED DIETARY ALLOWANCES (USRDA)

Vitamin A	4	4	4	4
Vitamin C	4	4	4	4
Calcium	4	4	4	4
Iron	4	4	4	4
Vitamin D	4	4	4	4
Vitamin E	4	4	4	4
Thiamine	4	4	4	4
Riboflavin	4	4	4	4
Niacin	4	4	4	4
Vitamin B6	4	4	4. . .	

DETD . . . life. The trial was also to monitor the safety of the Prepared Diet by monitoring nutritional intake in plasma vitamins (**Vitamin A** and Vitamin D) and mineral (iron), and trace minerals levels.

=> s l8 and polypeptide
L8 NOT FOUND
The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> d his

(FILE 'HOME' ENTERED AT 13:00:42 ON 23 APR 2003)

FILE 'USPATFULL' ENTERED AT 13:01:03 ON 23 APR 2003
L1 2113 S PALMITATE AND VITAMIN A
L2 1484 S L1 AND VITAMIN E
L3 894 S L2 AND VITAMIN C
L4 0 S L3 AND VITAMINB .SUB. 3
L5 99 S L3 AND VITAMIN B .SUB. 3
L6 21 S L5 AND PD<2000
L7 18 S L6 AND SKIN

```
=> s l7 and polypeptide
         44180 POLYPEPTIDE
L8           2 L7 AND POLYPEPTIDE

=> d l8 1-2

L8   ANSWER 1 OF 2  USPATFULL
AN     97:68148  USPATFULL
TI     Personal product compositions comprising heteroatom containing alkyl
       aldonamide compounds
IN     Vermeer, Robert, Nutley, NJ, United States
PA     Lever Brothers Company, Division of Conopco, Inc., New York, NY, United
       States (U.S. corporation)
PI     US 5653970              19970805                              <--
AI     US 1994-352008          19941208 (8)
DT     Utility
FS     Granted
LN.CNT 6060
INCL   INCLM: 424/070.240
       INCLS: 424/070.100; 514/847.000; 510/126.000; 510/135.000
NCL    NCLM:  424/070.240
       NCLS:  424/070.100; 510/126.000; 510/135.000; 514/847.000
IC     [6]
       ICM: A61K007-07
       ICS: A61K007-075
EXF    424/401; 424/70.31; 424/70.19; 424/70.24
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8   ANSWER 2 OF 2  USPATFULL
AN     97:53932  USPATFULL
TI     Hair care compositions comprising heteroatom containing alkyl aldonamide
       compounds
IN     Vermeer, Robert, Nutley, NJ, United States
PA     Lever Brothers Company, Division of Conopco, Inc., New York, NY, United
       States (U.S. corporation)
PI     US 5641480              19970624                              <--
AI     US 1994-352309          19941208 (8)
DT     Utility
FS     Granted
LN.CNT 5444
INCL   INCLM: 424/070.240
       INCLS: 424/070.100
NCL    NCLM:  424/070.240
       NCLS:  424/070.100
IC     [6]
       ICM: A61K007-07
       ICS: A61K007-075
EXF    424/70.1; 424/70.13; 424/70.17; 424/70.24
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> d l8 1 bib, kwic

L8   ANSWER 1 OF 2  USPATFULL
AN     97:68148  USPATFULL
TI     Personal product compositions comprising heteroatom containing alkyl
       aldonamide compounds
IN     Vermeer, Robert, Nutley, NJ, United States
PA     Lever Brothers Company, Division of Conopco, Inc., New York, NY, United
       States (U.S. corporation)
PI     US 5653970              19970805                              <--
AI     US 1994-352008          19941208 (8)
```

DT Utility
FS Granted
EXNAM Primary Examiner: Gardner, Sallie M.
LREP Koatz, Ronald A.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5653970 19970805 <--
AB The invention relates to personal product compositions containing heteroatom containing alkyl aldonamide compounds and **skin** conditioning agent. Unexpectedly, applicants have found that when these heteroatom containing alkyl aldonamides are used, benefits such as enhanced stability. . .
SUMM . . . For this reason, a special importance is attached in the cosmetic area to personal products particularly, bath preparations, cleansing preparations, **skin** care preparations, shaving preparations and deodorant or antiperspirant preparations.
SUMM The primary function of a personal product composition is to cleanse the **skin** gently without irritation or excessive defatting or overdrying the **skin**. In addition, successful personal product compositions should not leave the **skin** tight or taut after frequent routine use. After accomplishing the cleansing action, the personal product composition should leave the **skin** feeling soft, smooth, silky and moisturized while simultaneously providing a rich copious foam or lather. This has become a difficult. . . in making a totally satisfactory product. For one thing, it is known that certain mild surfactant systems when formulated for **skin** cleansing, often exhibit poor foam or low lather performance. On the other side, the use of high sudsing surfactants with lather boosters can yield acceptable lather volume, unfortunately however, such surfactant systems are usually harsh to the **skin**. It will be appreciated that these two factors make the formulation process, a delicate balancing act.
SUMM . . . a personal product composition of the invention, surprisingly provides improved foam, viscosity, clarity and conditioning characteristics while simultaneously making the **skin** feeling soft, smooth, silky and moisturized. These findings are quite unexpected and have not been recognized or appreciated in the. . .
SUMM . . . roll-on, stick, tablet, powdered and bar form. Included among the personal product compositions are bubble bathes, shower gels, body shampoos, **skin** cleansers or lotions, liquid soaps, toilet bars, syndet bars, sunscreens, shaving creams, deodorants or antiperspirants and the like.
SUMM . . . good shelf life and should not become turbid or produce sedimentation upon standing. Ideal personal product compositions should cleanse the **skin** gently and should not overdry the **skin**. Surprising the personal product compositions of the present invention that comprise a heteroatom containing alkyl aldonamide compound produce clear, stable,. . .
SUMM . . . alkyl carboxybetaines) and mixtures thereof, could result in a clear thickened personal product composition that foams copiously and leaves the **skin** feeling soft, smooth, silky and moisturized.
SUMM U.S. Pat. No. 4,973,473 to Schneider, et al. teaches **skin** treatment compositions in which the primary moisturizing agent may be a gluconamide compound. Methyloxypropyl gluconamide is the only example of. . .
SUMM These compounds are said to be useful as emollients which are substantive to **skin** or hair and are further taught in U.S. Pat. Nos. 3,990,991 to Gerstein, 4,534,964 to Herstein et al. and 4,529,588. . .

SUMM . . . the heteroatom containing alkyl aldonamide compounds of the invention in compositions with for example, certain essential ingredients such as cosurfactants, **skin** conditioning agents, **skin** feel mildness agents, suspending agents, hydroxy acids, auxiliary thickening agents and auxiliary agents (see claim 4). There is also clearly. . .

SUMM . . . object of the present invention to provide mild personal product compositions that efficiently remove surface grease and dirt from the **skin**.

SUMM It is still another object of the present invention to provide new and improved personal product compositions that leave the **skin** feeling fragrant, soft, smooth, silky and moisturized.

SUMM It is a final object of the present invention to provide an improved method of cleansing and conditioning the **skin**. These and other objects will become readily apparent from the detailed description which follows.

DETD . . . sought. Such ingredients are well known to those skilled in the art and include, but are not limited to cosurfactants, **skin** conditioning agents, **skin** feel mildness agents, suspending agents, hydroxy acids, auxiliary thickening agents, water and other optional ingredients (auxilary agents).

DETD . . . fatty acid halides. Suitable examples of hydrolyzable proteins include collagen, corn, keratin, silk, soy, scrapleather, wheat gluten and albumin. Preferred **polypeptide** amino acid salts useful in the present invention include the sodium, potassium and ammonium salts of dodecyl, tetradecyl, coconut and. . .

DETD Cationic surfactants have been taught in the art as conditioning agents for the **skin**. Suitable cationic surfactants are broadly exemplified as those of the general formula:

DETD **Skin** Conditioning Agents (Moisturizers/Emollients)

DETD Various materials have been taught in the art for use as agents that condition the **skin**. In general, such conditioning agents are designed to make the **skin** feel soft, smooth, silky and moisturized.

DETD . . . term emollient, and is meant to describe a material which imparts a soft, smooth, silky and moisturized feeling to the **skin** surface.

DETD One way of moisturizing is to reduce the rate of water loss from the stratum corneum (**skin** surface) by depositing an occlusive material (emollient or emulsifier) on the **skin** surface which prevents water evaporation. Mother technique is to add hygroscopic nonocclusive substances (humectants), which will retain water to the stratum corneum, making water available to the **skin** surface thereby producing the desired cosmetic effect. Nonocclusive moisturizers also function by improving the lubricity of the **skin**. Both occlusive and nonocclusive moisterizers as well as mixtures thereof are operative in the present invention. Examples of occulusive moisturizers.. . . include polyols, fatty acids, certain alkanolamides, pyrrolidone carboxylic acid and their derivatives. It is to be understood that any such **skin** conditioning agent or mixtures thereof can be employed herein, depending on the formulations desires.

DETD . . . decyl neopentanoate, myristyl propionate, decyl oleate, isopropyl myristate, lauryl myristate, myristyl myristate, myreth-3-myristate, palmityl myristate, stearyl myristate, isopropyl palmirate, octyl **palmitate**, 2-ethylhexyl palmirate, lauryl **palmitate**, myristyl palmirate, palmityl **palmitate**, stearyl palmirate, butyl stearate, myristyl stearate, palmityl stearate, isocetyl stearate, isostearyl isostearate, oleyl myristate, oleyl stearate, oleyl oleate, methyl cocoate,. . . butanediol, PPG-8-C.sub.12 -C.sub.20 alkyl ester, Peg-45 palm kernel glyceride, neopentylglycol dicaprylate/dicaprate, C.sub.12 -C.sub.15 alcohol

benzoate, diisoarachidyl dilinoleate, dioctyl maleate, ascorbyl **palmitate**, diisopropyl adipate, diisohexyl adipate, dihexadecyl adipate, diisopropyl sebacate, dioctyl succinate, didecyl succinate, jojoba esters and the like.

DETD . . . potassium, ammonium and alkanol ammonium salts of pyrrolidone carboxylic acid, ethyl pyrrolidone carboxylic acid and the like. Typical levels of **skin** conditioning agent are from about 1% to about 40%, preferably from about 2% to about 30%, even more preferably from. . .

DETD **Skin** Feel Mildness Agents

DETD The **skin** feel mildness agents useful in the present invention include, but are not limited to the cationic, anionic, amphoteric and nonionic polymers used in the cosmetic field. Reduced **skin** irritation benefits of cationic and nonionic polymers are described in Polymer JR for **Skin** Care Bulletin, by Union Carbide in (1977). The cationic polymers also provide a desirable soft, smooth and silky feeling to the **skin**. While wishing not to be bound to theory, it is believed that cationic polymers chemically interact with anionic surfactants to form complexes which may enhance overall mildness to **skin** characteristics. Also, there is a reason to believe that positively charged cationic polymers can bind with negatively charged sites on the **skin** to provide a softer **skin** feel after use. The cationic polymers are most preferred because they provide the best **skin** feel benefits.

DETD . . . in the present invention is discribed in U.S. Patent No. 4,438,095 which is incorporated herein by reference. Typical levels of **skin** conditioning agent are from about 0% to about 5%, preferably from about 0% to about 4%, even more preferably from. . .

DETD Hydroxy acids have been taught in the art for use as agents that exfoliate dead **skin** cells leaving **skin** smoother and tighter with a more youthful appearance. In addition, hydroxy acid treatments help reduce liver and sun spots as. . .

DETD . . . and vegetables or by fermentation of corn or sugar substrates) and the like are useful as well. Typical levels of **skin** conditioning agent are from about 0% to about 10%, preferably from about 0% to about 8%, even more preferably from. . .

DETD Various materials have been taught in the art as agents that are useful in suspending certain performance ingredients such as **skin** feel mildness agents, silicone fluids, and the like, uniformly, thereby assisting in the delivery of the desirable performance attributes associated. . .

DETD Examples of sunscreens or UV absorbers useful in the present invention which protect the **skin** and certain sensitive ingredients from harmful sunlight include dipropyleneglycol salicylate, octyl salicylate, 2-ethylhexyl p-dimethylaminobenzoate (octyldimethyl-PABA), polyoxyethylene p-dimethylaminobenzoate (PEG-25 PABA), Tri-PABA-panthenol,. . .

DETD Examples of vitamins useful in the present invention which provide the hair with valuble nutrition include **vitamin A** (as retinyl acetate, propionate or **palmitate**) provitamin A (based on carrot extract, as .beta.-carotene), vitamin B.sub.1 (as thiamine mononitrate), vitamin B.sub.2 (as riboflavin), **vitamin B.sub.3** (as niacinamide), vitamin B.sub.5 (as pantothenic acid), provitamin B.sub.5 (as panthenol), vitamin B.sub.6 (as pyridoxine hydrochloride, dioctenoate, dilaurate, dipalmitate or tripalmitate), vitamin B.sub.12 (as cyanocobalamin), vitamin B.sub.15 (as pangamic acid), **vitamin C** (as ascorbic acid), vitamin D.sub.2 (as ergocalciferol), vitamin D.sub.3 (as cholecalciferol), **vitamin E** (as dl-.alpha.-tocopherol acetate, linoleate or nicotinate,), vitamin F (as glyceryl linoleate and glyceryl linolenate), vitamin K.sub.1 (as phytonadione), vitamin K.sub.3. . . bioflavoniod and mixtures thereof. Preferred

vitamins are provitamin A, vitamin B.sub.1, vitamin B.sub.2, provitamin B.sub.5, vitamin B.sub.6, vitamin B.sub.12 and **vitamin E**. Typical levels of vitamin are from about 0% to about 7% by weight of the composition.

DETD Examples of amino acids useful in the present invention which provide the **skin** with valuble nutrition include alanine, .beta.-alanine, N-methylalanine, N-phenylalanine, .alpha.-aminoisobutyric acid, .alpha.-aminobutyric acid, .alpha.-aminocaproic acid, .epsilon.-aminocaproic acid, glycine, N-ethylglycine, N-propylglycine, N-butylglycine,. . . (keratin polypeptides), silk amino acids, allantoin acetyl methionine, allantoin, deoxyribonucleic acid, protamine/nucleic acid complex, nucleic acid, collagen amino acids, retinyl **palmitate polypeptide**, proline, polyglucan and mixtures thereof. Preferred amino acids are glycine, methionine, sarcosine, keratin amino acids and silk amino acids. Typical. . .

DETD Examples of proteins useful in the present invention which provide the **skin** with valuble nutrition include hydrolyzed casein, hydrolyzed collagen (hydrolyzed animal protein), myristoyl hydrolyzed animal protein, hydrolyzed corn protein, hydrolyzed glycosaminoglycans,. . .

DETD . . . present invention which prevent the oxidation of certain ingredients by air and prevent the development of unpleasant, rancid odors include **vitamin E** (tocopherol), lecithin, wheat germ oil, sodium sulfite, sodium bisulfite, uric acid, propyl gallate, butylated hydroxyanisole (BHA), toluhydroquinone (THQ) sold as. . .

DETD . . . adjusted to a pH of about less than 7 to provide a composition that is non-irritating and non-damaging to the **skin** of the consumer. The amount of buffering agent used will be that which is sufficient to provide the desired buffered. . .

DETD Examples of heeling agents which function to stimulate the growth of healthy **skin** tissue include allantion, aluminum dihydroxy allantoinate, urea, uric acid, aloe vera gel, methyl manuronate, uronic acids, sucrose octaacetate, menthol, hydrolyzed. . .

DETD (c) from about 1% to about 40% by weight of the composition is a **skin** conditioning agent;

DETD (d) from about 0% to about 5% by weight of the composition is a **skin** feel mildness agent;

DETD (c) from about 2% to about 30% by weight of the composition is a **skin** conditioning agent;

DETD (d) from about 0% to about 4% by weight of the composition is a **skin** feel mildness agent;

DETD (c) from about 3% to about 25% by weight of the composition is a **skin** conditioning agent;

DETD (d) from about 0% to about 3% by weight of the composition is a **skin** feel mildness agent;

DETD (c) from about 3.1% to about 25% by weight of the composition is a **skin** conditioning agent;

DETD (d) from about 0% to about 3% by weight of the composition is a **skin** feel mildness agent;

DETD . . . in a variety of types and forms. A classification according to product type would consist of bath products, cleansing products, **skin** care products, shaving products and deodorant/antiperspirant products.

DETD Examples of **skin** care products include, but are not limited to hand/body/facial moisturizers, hand/body/facial creams, massage creams, hand/body/facial lotions, sunscreen products, tanning products,. . .

DETD . . . the heteroatom containing alkyl aldonamide compounds of the invention are useful as foam stabilizing agents, thickening agents, solubilizing agents and **skin** conditioning agents. In addition, it has been found that the heteroatom containing alkyl aldonamide

compounds of the invention are also. . .

DETD The present compositions are used in a conventional manner for cleaning and/or conditioning the **skin**. From about 0.1 g to about 15 g of a composition is applied to the **skin** that may or may not be thoroughly wetted with water. The composition is worked unto the **skin** from about 30 seconds to about five minutes and then rinsed off or left on.

DETD The zein solubilization assay was developed to determine the biological effects of surfactants on the **skin**. The protein is normally in soluble in water, but can be brought into solution by interaction with surfactants. The extent. . . Z. Poly., 233, 848, 1969). The greater the zein solubilization, the greater the irritation potential of that surfactant on the **skin**.

DETD In order to demonstrate the improved ability of heteroatom containing alkyl aldonamide to provide mildness benefits to the **skin**, mixtures of C.sub.8 /C.sub.10 oxypropyl D-gluconamide (C.sub.8 /C.sub.10 OPG) and sodium lauryl sulfate (SLS) by weight were tested and compared. . .

DETD . . . so the heteratom containing alkyl aldonamide compounds not anly enhance viscosity and stabilize foam, but are also mild to the **skin**.

DETD High Foaming **Skin** Conditioning Bubble Bath

DETD High Foaming **Skin** Conditioning Bubble Bath Concentrate with Protein

DETD . . . Laurate

13. PEG-30 Glyceryl -- -- -- -- -- -- 4.0 Cocoate

14. PEG-200 -- -- -- -- -- -- 4.0 Glyceryl **Palmitate**

15. Glyceryl Laurate 1.0 -- -- -- -- -- --

16. C8/C10 1.0 -- -- -- 1.0 -- 1.0 Oxypropyl D-Gluconamide

17.. . . 3.0 --

32. Hena Extract -- -- -- -- -- 0.5 --

33. Tocopherol -- 0.5 -- -- -- -- 1.0 Acetate (**Vitamin E**)

34. Panthenol 0.5 -- -- -- -- -- -- (Vitamin B5)

35. Ethylene Glycol -- -- 0:6 -- -- -- -- Monostearate

36.. . .

DETD . . . -- 0.6 -- --

31. Panthenol -- -- -- 2.0 -- -- -- (Vitamin B5)

32. Tocopheryl -- -- -- 2.0 -- -- -- Acetate/Linoleate (**Vitamin E**)

33. Butylated 0.01 0.01 -- -- -- 0.1 -- Hydroxytoluene

34. Carboxymethyl -- -- -- 1.5 -- -- -- Cellulose

35. Hydroxyethyl
-- -- --. . .
DETD . . . 2.0 --
27. Kelp Extract
-- -- -- -- -- -- 2.0
28. Tocopheryl Ace-
-- -- -- -- -- -- 0.5
tate (**Vitamin E**)
29. Sodium 5.0 5.2 -- -- 5.0 -- --
Isethionate
30. Sodium Chloride
0.5 0.5 0.5 0.5 0.4 -- --
31. Titanium Dioxide
0.5. . .
DETD A Mild Moisturizing Syndet Bar Composition with **Vitamin E** and Bath Oil
DETD . . . -- --
Protein
54. TEA-Coco
-- -- -- -- -- -- 18.0
Hydrolyzed Animal
Protein
55. Tocopheryl Ace-
-- -- -- -- -- -- 0.3
tate (**Vitamin E**)
56. Sodium -- 0.2 -- -- 0.3 -- --
Dehydroacetate
57. Sodium Pyrroli-
-- -- -- -- -- 4.0 --
done Carboxylic Acid
58. Disodium. . .
DETD An Astringent Facial Cleansing Composition with Protein, **Vitamin E** and Aloe
DETD . . . Acetylated Lanolin
-- -- 0.2 -- -- -- --
Alcohol
31. C.sub.12 -C.sub.15 Alcohol
-- -- 0.4 -- 4.0 -- --
Benzoate
32. Octyl **Palmitate**
-- -- -- -- -- 2.5 --
33. Methyl Glucose -- -- 0.8 -- -- --
Sesquistearate
34. Diisoarachidyl
-- -- 1.0 -- -- -- --
Dilinoleate
35. Dioctyl Maleate
-- -- -- -- 5.0 -- --
36. Ascorbyl **Palmitate**
-- -- -- 0.1 -- -- --
37. Stearic Acid (xxx)
-- -- 0.5 -- 1.0 1.0 --
38. Isostearic Acid
-- -- -- -- -- 1.7 --
39. Tocopheryl Ace-
-- -- -- 0.2 -- 0.1 1.0
tate (**Vitamin E**)
40. Panthenol
-- -- -- -- -- -- 1.0
(Provitamin B5)
41. Retinyl **Palmitate**
-- -- 3.0 -- -- -- --

```
retenyl palmatate
RETENYL IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s retenyl palmatate?
             1 RETENYL
            76 PALMATATE?
L1           0 RETENYL PALMATATE?
                 (RETENYL(W)PALMATATE?)

=> s retinyl palmatate?
           853 RETINYL
            76 PALMATATE?
L2           1 RETINYL PALMATATE?
                 (RETINYL(W)PALMATATE?)

=> d l2 bib, kwic

L2   ANSWER 1 OF 1  USPATFULL
AN     2003:57104  USPATFULL
TI     Trans dermal skin care
IN     Gulla, Michael, Sarasota, FL, UNITED STATES
       Goldberg, Robert L., Sharon, MA, UNITED STATES
PA     Neo Tech Development Company, L.L.C., Sharon, MA (U.S. corporation)
PI     US 2003039668      A1   20030227
AI     US 2002-86990      A1   20020301 (10)
PRAI   US 2001-274359P     20010308 (60)
DT     Utility
FS     APPLICATION
LREP   Robert L. Goldberg, 56 Wilshire Street, Sharon, MA, 02067
CLMN   Number of Claims: 20
ECL    Exemplary Claim: 1
DRWN   No Drawings
LN.CNT 1094
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD   . . . and contained aloe babadensis and minor amounts of conventional
       additional components such as propylene glycol, glycerin, polysorbate
       20, tocopheryl acetate, retinyl palmatate,
       pantherol, matricaria extract, jojoba oil, carbomer 940,
       trietheranolamine, diazoolidinyl urea, propylparaban, methylparaban,
       disodium EDTA, and various fragrances. There was no. . .


=>
```

CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> s ascorbylmethyl silanol
L1 0 ASCORBYLMETHYL SILANOL

=> s ascorbylmethylsilanol
L2 1 ASCORBYLMETHYLSILANOL

=> d l1
L1 HAS NO ANSWERS
L1 0 SEA ASCORBYLMETHYL SILANOL

=> d l2

L2 ANSWER 1 OF 1 USPATFULL on STN
AN 2002:42939 USPATFULL
TI COSMETIC AND/OR DERMATOLOGICAL COMPOSITION CONTAINING A DERIVATIVE OF METHYLATED SILANOL AND A DERIVATIVE OF HYDROLYSED PLANT PROTEIN
IN FRUCTUS, ALAIN E, COURBEVOIE, FRANCE
MONTET, FLORENCE, LEVALLOIS PERRET, FRANCE
LAZAR, GABRIELA, HAMBURG, GERMANY, FEDERAL REPUBLIC OF
TOKGOZ, NUR SELCAN, PARIS, FRANCE
PI US 2002025303 A1 20020228
AI US 1999-381976 A1 19991203 (9)
WO 1998-EP2115 19980331
PRAI FR 1997-4167 19970404
DT Utility
FS APPLICATION
LN.CNT 1011
INCL INCLM: 424/078.030
INCLS: 424/401.000; 514/002.000; 514/063.000; 514/844.000
NCL NCLM: 424/078.030
NCLS: 424/401.000; 514/002.000; 514/063.000; 514/844.000
IC [7]
ICM: A01N037-18
ICS: A61K038-00; A61K031-695; A01N055-00; A61K031-74; A61K006-00; A61K007-00; A01N025-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l2 1 kwic

L2 ANSWER 1 OF 1 USPATFULL on STN
DETD [0036] **ascorbylmethylsilanol** (Ascorbosilane concentrate C.RTM., Exsymol)
DETD [0037] **ascorbylmethylsilanol** pectinate (Ascorbosilane C.RTM., Exsymol)
DETD [0062] **ascorbylmethylsilanol**,
DETD [0063] **ascorbylmethylsilanol** pectinate,
DETD . . . or ascorbyl and disodium sulphate (Nikkol VC-SS.RTM., Jan Dekker) or ascorbyl palmitate or ascorbic acid polypeptide (Vitazyme C.RTM., Brooks) or **ascorbylmethylsilanol** pectinate (Ascorbilane.RTM., Exsymol) or microspheres whereof the wall is made of carraghenine encapsulating vitamin C (Lipotec) or microspheres whereof the. . .

L1 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 177799-59-6 REGISTRY
CN Retinol, hexadecanoate, mixt. with Vitazyme C and Vitazyme E (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Vitazyme C, mixt. contg. (9CI)
CN **Vitazyme E, mixt. contg. (9CI)**
OTHER NAMES:
CN **Vitazyme ACTN**
FS STEREOSEARCH
MF C36 H60 O2 . Unspecified . Unspecified
CI MXS
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 177698-62-3
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

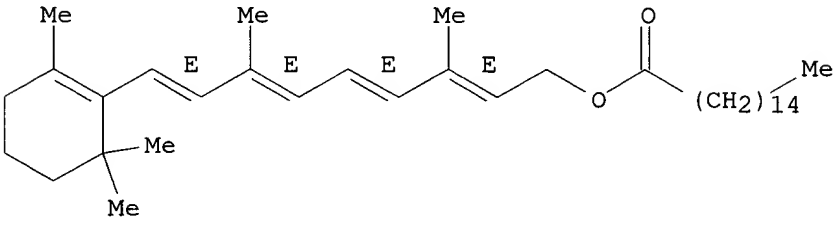
CRN 167973-55-9
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 3

CRN 79-81-2
CMF C36 H60 O2

Double bond geometry as shown.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 177698-62-3 REGISTRY
CN **Vitazyme E (9CI)** (CA INDEX NAME)
MF Unspecified
CI COM, MAN
SR CA

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

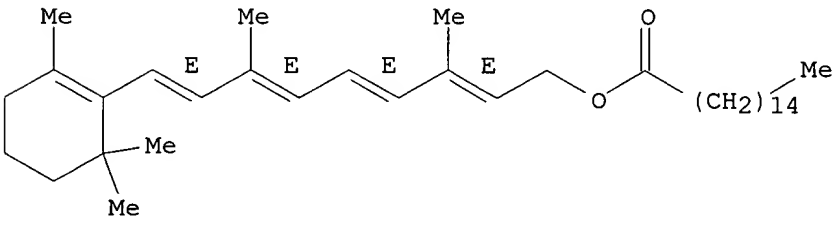
L1 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 167973-55-9 REGISTRY

CN **Vitazyme C (9CI)** (CA INDEX NAME)
MF Unspecified
CI COM, MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 79-81-2 REGISTRY
CN Retinol, hexadecanoate (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Retinol palmitate (6CI, 7CI)
CN Retinol, palmitate, all-trans- (8CI)
OTHER NAMES:
CN all-trans-Retinol palmitate
CN all-trans-Retinyl palmitate
CN all-trans-Vitamin A palmitate
CN Aquapalm
CN Aquasol A
CN Arovit
CN Arovit (Roche)
CN Axerophthol palmitate
CN Dispatabs Tabs
CN Lutavit A 500 Plus
CN Myvak
CN Myvax
CN Palmitic acid, ester with retinol
CN Retinyl palmitate
CN Testavol S
CN trans-Retinol palmitate
CN trans-Retinyl palmitate
CN Vitamin A palmitate
CN **Vitazyme A**
FS STEREOSEARCH
DR 7488-89-3, 37340-08-2, 108066-99-5
MF C36 H60 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1983 REFERENCES IN FILE CA (1967 TO DATE)
16 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1986 REFERENCES IN FILE CAPLUS (1967 TO DATE)
62 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

Polypeptide
42. Lecithin
-- -- 10.0 -- -- -- --
43. Proline -- -- -- -- 1.0 -- --
44. Polyglucan
-- -- 0.1. . .
DETD A Moisturizing Lotion Composition with Antioxidants for Aging **Skin**
DETD A Moisturizing Cream Composition with Alpha Hydroxy Acids and **Vitamin E**
DETD . . . -- --
(2%)
46. Carbomer 940
-- -- -- -- -- 10.0 5.0
(2%)
47. Tocopheryl Ace-
-- -- -- 0.1 0.2 -- 0.2
tate (**Vitamin E**)
48. Ascorbic Acid
-- -- -- -- 0.3 -- --
(**Vitamin C**)
49. Ascorbyl **Palmitate**
-- -- -- -- -- -- 0.2
50. Retinyl **Palmitate**
-- -- -- -- -- -- 0.3
(**Vitamin A**)
51. Bioflavoniod
-- -- -- -- -- -- 0.4
52. Ivy Extract
-- -- -- -- -- -- 0.9
53. Dimethicone
-- --. . .
DETD A Sunscreen Cream Composition with **Vitamin E**
DETD A Sunscreen Cream Composition with **Vitamin E**
DETD . . . --
35. Animal -- -- -- 0.5 0.1 -- --
Collagen
(Soluble)
36. Tocopheryl -- -- -- -- 0.1 -- --
Acetate
(**Vitamin E**)
37. Acetamide -- -- -- 1.5 -- -- --
MEA
38. Lactamide -- -- -- 1.5 -- -- --
MEA
39. Allantoin --. . .
DETD A Nonalcoholic Aftershave Lotion Composition with **Vitamin E**
DETD An Aftershave **Skin** Conditioning Composition
CLM What is claimed is:
. . . ammonium chloride, sodium sulfate, potassium sulfate, magnesium sulfate, sodium isethionate, sodium thiosulfate and mixtures thereof; (d) about 1% to 40% **skin** conditioning agent; and (e) water.